# BERI-BERI

*RESEARCHES CONCERNING ITS NATURE AND CAUSE*
*AND THE MEANS OF ITS ARREST*

MADE BY ORDER OF THE NETHERLANDS GOVERNMENT

BY


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*WITH COLOURED ILLUSTRATIONS FROM ORIGINAL DRAWINGS*


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EDINBURGH : TEVIOT PLACE. LONDON : 38 WEST SMITHFIELD, E.C.

# PREFACE TO THE FRENCH EDITION.

THE researches as to the nature and cause of Beri-beri, of which we are giving a description in the following pages, have been made by order of the Netherlands Government, on account of the sad ravages caused by the disease in the ranks of both army and navy, in the neighbourhood of Atjeh, a district lying in the north-west of the island of Sumatra.

The object of this expedition was to try to discover, by better acquaintance with the disease in every phase, more positive means of combating it than any in use up to the present day.

With this end in view we started for the Indies, where we remained eight months, from the end of November 1886 to the beginning of August 1887. We stayed in Batavia until the end of January—a very good position for a laboratory being assigned to us in the large military hospital of Weltevreden. From the 19th of February to the beginning of May we were installed at Atjeh, and there too an excellent laboratory was placed at our disposal in the hospital of Pauteh Perak. On our journey from Batavia to Atjeh we had the opportunity of a fortnight's visit to Padang; we also made excursions to Kajoutanam and Fort de Kock. We found several Beri-beri patients in the military hospital at Padang who had just arrived from Atjeh; also convalescents, in different stages of recovery, in two other places.

Early in May we returned to Batavia, and continued our work in the laboratory of Weltevreden, until our departure for Europe.

It is pleasant to us to be able to express our gratitude, not only to Government, which put at our disposal every necessary

aid to the work, but also for the valuable help given by our colleagues, military and civil, and a number of friends quite strangers to the study of medicine. It is true, we had allowed ourselves to count a little on their interest, but never for one moment on support so largely and generously given.

Amongst those to whom we are under the greatest obligations we may name Colonel van Teyn, Civil and Military Governor of the province of Atjeh and its dependencies.

We owe, too, special thanks to MM. C. Eykman and M. B. Romeny, military doctors, who were associated with us in our work, and who showed not only great talent but devotion in the performance of the task allotted to them.

We have endeavoured, in as concise a manner as the subject will allow, to give a description of the information gained by these researches.

Every one who has made any study of Beri-beri, will readily understand that the task committed to us was both an extensive and a difficult one. Our chief aim was to try and obtain a practical result, and in this we hope we have succeeded, and think we are able by the researches made to establish a clearer idea as to the nature of the malady than any hitherto known. As will be gathered from a description of the cases in the chapters on both the clinical and pathological phases of the disease, we believe we have proved the truth of the hypothesis, until now only considered as probable, that Beri-beri is a multiple peripheral neuritis. We had, however, a keynote, which allowed us to confirm a theory, which, if in keeping with the origin of Beri-beri at all, might be considered as the cause of the disease. In fact, the micrococci found in the blood of Beri-beri patients, and cultivated by us, produced in animals a multiple peripheral neuritis.

Besides, our experience has given us strong reason to believe in the opinion already advanced, that a living organism is the cause of Beri-beri, and is found in the air of the districts where the malady actually exists.

We thus acquired the conviction that it would be necessary to find the sure means of combating the malady by the destruction of these living organisms, or that, in other words, by the employment of disinfection, we might expect the best re-

sults, especially if the necessary disinfections were carried out in the buildings where persons became actually affected.

We have indicated clearly, or at least hope so, in the description of our work, the manner in which we arrived at these conclusions. We have tried to give our readers all the information necessary to explain and support our opinions, without wearying them with details of cases, autopsies, the numerous experiences and interesting materials, "rudis indigestaque moles," out of which the experimentalist is himself obliged to make a choice.

We have not cited all that we have ourselves read in the works on Beri-beri, to enable us to form an opinion, but only what we considered necessary to render our communications clear.

Those who would wish to know more of Beri-beri will find ample information on the subject in the works of M. van Overbeek de Meyer,[1] M. Leroy de Méricourt,[2] M. Roux,[3] M. Corre,[4] and M. van der Burg.[5]

We have no other aim than to give a description of the researches made, and to indicate not only the positive results, in which we ought to rejoice, but also the lacunae, of which we are as well aware as any one can be.

This is why we have thought that moderation in our explanations was absolutely necessary.

[1] Geneesk Tijdschr. v. d. Zeemacht, 1865, p. 1.

[2] Diction. Encycl. des Sciences Méd., 1868, Art. Beri-beri, p. 129.

[3] Traité pratique des maladies des pays chauds. Paris, 1868, p. 470.

[4] Traité clinique des maladies des pays chauds. Paris, 1887, p. 151.

[5] De geneesheer in Ned. Indië, Batavia, 1887, vol. ii., p. 444.

# PREFACE TO THE ENGLISH EDITION.

THE frequent occurrence of cases of Beri-beri in the out-patient department of the Alice Memorial Hospital, Hong Kong, led me to look up the literature of the subject. Until I chanced upon the work of Pekelharing and Winkler, I met with no attempt to deal with the disease in a scientific manner nor indeed with any degree of breadth or fulness. Next in importance is the result of the work of the German doctors connected with the Tokio University, Japan, where, after careful investigation, Kakké was proved to belong to the genus Beri-beri. Amongst British observers few have done anything beyond recording cases, and contributing a few unimportant papers. Latterly, however, Surgeon-Captain J. T. W. Leslie, M.B., of the Indian Medical Service, in Burmah, has produced a valuable brochure on the disease; and, in Assam, Surgeon-Major G. M. J. Giles, M.B, of the same service, has been dealing with the subject by the methods of recent investigation, and has contributed many details and observations. Giles has been caught, as many have been before, by the worm theory of the genesis. This no doubt he will modify as time goes on, or, if not, his successors in the field will do so. One is proud of Giles' work, however, as a record of careful scientific labour, and it lies with others to prove the faulty and unstable nature of his conclusions.

Simon of Singapore has done much towards abolishing the worm theory, even with the scientific dress of Giles. Walker of Borneo, who is a keen investigator from the duodenal worm point of view, writes to me to be careful not to place him in the list of believers in that theory. I must add my own testimony, to the effect that I have not found the *Ankylostoma duodenale* in

the evacuations of Beri-beri patients in Hong Kong, nor in the intestines after death. That intestinal worms can cause nervous symptoms of a reflex nature we all know, but that they can cause acute degeneration of the peripheral nerves we cannot believe. The translation of this work has not been undertaken with a view to profit, but in the belief that it is of national importance to have the standard work on the subject available in the language which, scientifically, prevails in the countries where Beri-beri is most widely met with: Ceylon, Assam, Burmah, the Malay Peninsula, Singapore, Borneo, Hong Kong, Japan, &c.

To Mr H. L. Dennys, of Hong Kong, most of the labour of translation has fallen; and to him, to Surgeon-Captain William Wilfrid Webb, M.B., of the Bengal Army, who has kindly seen the work through the press, and to Miss A. Thompson, of the Peak Hospital, Hong Kong, my thanks are due.

JAMES CANTLIE.

HONG KONG, 1893.

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# BERI-BERI.

# BOOK I.

# CLINICAL OBSERVATIONS.

# THE NATURE AND CAUSE OF BERI-BERI.

## CHAPTER I.

### DEFINITION OF BERI-BERI.

WHEN we left Holland for the East Indies, we were aware that we were about to become acquainted with a disease having many and varied symptoms. Even the mere attempt to unravel the truth, as to the origin and derivation of the word Beri-beri, at once showed us a difficulty at the very threshold of our investigations. After careful search we cannot now give the exact etymology of the name, but, of the many suggestions, we naturally incline to those words which seem to have arisen from a study of the most striking symptoms peculiar to the disease.

According to Bontius,[1] it was the peculiar style of walk, stiff and tottering, that suggested the term. He tells us that the word *Bhayree* means a sheep in Hindustani, and, that the gait in beri-beri reminds one of the stiff gait of the sheep.

Marshall,[2] on the other hand, says that *Bhayree* signifies weakness, and the repetition of the word, extreme weakness. According to Malcolmson,[3] however, *Bhayree* in Hindustani

[1] Bontius. De medicina Indorum, lib. iii., cap i. De paralyseos quadam specie quam Indigenæ beri-beri vocant. 1645.

[2] Marshall. Notes on the Topography of the Interior of Ceylon, p. 161; London, 1822.

[3] Malcolmson. Pract. Essay on the History and the Treatment of Beri-beri. Madras, 1838.

means great weakness, but only in the combination *Soon-bhayree.* Herklots,[1] for his part, thinks it quite possible that the Hindustani word *bhar-bari*, signifying swelling, has become corrupted into beri-beri, but adds that the great objection against these derivations from Hindustani is, that in no writing in that language can one find any trace of a description of this disease. Finally, Carter [2] assures us that asthma is the principal symptom of beri-beri, and derives it from the Arabic, in which language *bhur* means dyspnœa, and *bhari* a sailor; consequently beri-beri would mean "sailor's asthma."

We believe that what we have just said as to these etymological derivations will be sufficient, although it would be easy to increase the number. It seems impossible to settle the question, and by reference to it we only wished to call attention to the fact, that if the name of beri-beri might sometimes indicate stiffness or paralysis, sometimes weakness, swelling, or dyspnœa, it would clearly show that the prominent symptoms vary; thus in some cases difficulty in motion, in others general weakness, and yet again œdema and dyspnœa, are the most salient points in the clinical aspects of the disease.

In opposition to those who with Bontius consider paralysis the principal symptom and often do not make the least mention of œdema, are those who mention acute œdema (Fayrer, 1873), progressive anæmia, asthmatic dropsy, and sailors' asthma, and who relegate a secondary place merely to the troubles relating to motion.

Considering the foregoing statements, one cannot be surprised that the various authors who have treated of this subject have been so long in agreeing. When one sees that some have regarded it as relating to difficulties of movement only, whilst on the other hand some have regarded it as an affection of the respiratory organs, and others again referred the seat of the disease to the heart or circulatory system generally, the marvel is that such a heterogeneous group of symptoms should ever have come to be recognised as constituting one disease.

[1] Herklots. Compare Leroy de Méricourt. Diction. encyclop. des sciences médicales, p. 129, Art. Beri-beri, 1868.

[2] Carter. Beri-beri among the Marines of the Indian body of H. C. surveying vessels, *Palinurus* and *Nerbuddha*. Transactions of the Bombay Medical and Physical Society, No. 8, 1847.

This diversity of opinion was so great in 1861, that Fonssagrives and Méricourt[1] speak of a "deplorable war of words" and of a "reciprocal confusion." In order to put an end to this, these two savants proposed to distinguish in beri-beri two diseases, nearly related indeed, but still quite distinct from each other.

Contrary to the opinions of Scott, Copland, and Mason Good, these authors find in Bontius the description of a paralytic disease to which they give the name of "barbiers," but not of beri-beri, because the distinguishing character of the latter is considered to be the presence of exudations of serum beneath the skin, and into the sheaths of muscles and the cavities of the serous membranes.

The difficulty which always presents itself afresh in the clinical history of beri-beri was by such a division clearly indicated; but the attempt made to clear it was not a happy one, and threatened to make the confusion still greater. That this did not happen is due to the excellent observers who have known how to bridge the gap, which seemed insurmountable, between the two extreme forms under which beri-beri appears.

The credit of having drawn attention to the mixed form of beri-beri, and to the connection that exists between the paralytic and the dropsical varieties, belongs to Oudenhoven,[2] Da Sylva Lima,[3] and Overbeck de Meyer.[4] Oudenhoven introduces between atrophic beri-beri and dropsical beri-beri a polysarcous form, to which too little attention has been paid.

In very early accounts of the disease, as given by Da Sylva Lima, the mixed form was regarded as the most common.

Overbeck de Meyer attempted to fill up the gap by four intermediate forms. We shall only say here, that he is one of the

[1] Fonssagrives et Leroy de Méricourt. Archives gén. de médecine. Série v., vol. xviii., p. 287.

[2] Oudenhoven. Ned. Tijdschr. v. Geneesk., 1848, p. 577.

[3] Da Sylva Lima. Contribuiçao para a historia de una molestia que reine actualmente na Bahia, &c. Gazeta medica da Bahia, 1866-1867.
*Ibidem.* Essaio subre o beri-beri na Bresil, 1873. Compare: Archiv. de méd. navale, 1867, p. 150.
M. le Dr Larrey à propos du rapport présenté par M. le Dr Henri Dumont, et la traduction de l'art. de M. da Sylva Lima; Edinburgh Medical Journal, xviii., 2, Mars, pp. 831-845.

[4] Overbeck de Meyer. *See* note i. to Introduction, p. ix.

few observers who admits a convulsive form of beri-beri, a form which, according to our opinion, is of some importance. When in 1868 Leroy de Méricourt wrote his celebrated article in the *Dictionnaire de Médecine*, he had abandoned his previous notions of there being two diseases under one name. Agreement was at last arrived at when it came to be understood that the beri-beri of our East Indian Colonies, the *barbiers* of Mauritius, the *morbus innominatus* or sugar-works-sickness of Bahia, the "bad sickness" of Ceylon, were only different names for the same disease; and that they comprehended all the varieties described under the names dropsical asthma and pernicious œdema.

Some observers in Japan, Wernich,[1] Scheube,[2] Baelz,[3] and others, afterwards showed, in spite of the important opposition of Hoffmann,[4] that the disease *kakké* of that country is identical with beri-beri.

We are bound to make this digression into the field of history, because it was necessary to fix the point which previous observers had reached before we started for the East to investigate still more closely this terrible scourge of the Dutch Indies. There has been, so to speak, a halt in our knowledge of the disease since 1868.

Our starting point, therefore, consisted in this, that the symptomatology was well nigh exact, and that a clear definition was before us. Beri-beri, we learnt, was a disease characterised by difficulties in movement, frequently associated with an atrophic paralysis, especially of the lower limbs, by some slight disorders of sensibility, by œdema beneath the skin and of the muscles of the lower extremities, to which might be added dropsy of the serous cavities. In one series of cases nervous

[1] Wernich. Klinische Untersuchungen über die Japanische Varietät der Beri-Beri-Krankheit. Virchow's Archiv, vol. xxi., p. 290, 1876.
*Ibidem.* Ueber die Beziehungen zwischen Sogenannter perniciösen Anæmie und Beri-Beri-Krankheit. Deutsches Archiv für klinische med., vol. xxi., p. 108, 1877.

[2] Scheube. Die Japanische Kakke. Deutsches Archiv für klin. med.; vol. xxxi., p. 140-202. Ibidem, vol. xxxii., p. 83-119, 1882.
*Ibidem.* Weitere Beiträge zur pathologischen Anatomie und Histologie der Beri-beri. Virchow's Archiv, vol. xcv., p. 446, 1882.

[3] Baelz. Mittheilungen der deutschen Gesellschaft für Natur- und Völkerkunde Ostasiens, 1882.

[4] Hoffmann. Mittheilungen der deutschen Gesellschaft für Natur- und Völkerkunde Ostasiens, Fasc. 2, p. 16, 1873.

phenomena, properly so called, predominate, whilst in another the circulatory system seems to be the seat of primary pathological deviation. In still a third set, these symptoms appear simultaneously. If one compares this definition with that which one finds in one of the most recent treatises, as, for example, the work by Corre, one will see that it has not changed much since then. "Beri-beri," says this author, "is a disease characterised symptomatically by weakness, numbness and stiffening of the extremities, by certain alterations in sensibility, by difficult breathing, often also by œdema or a general puffiness, &c. . . . a disease with a sudden or gradual commencement, progressing rapidly or slowly, accompanied by relapses and recurrences."

Having got the symptomatology exact, one wished for more. It was absolutely necessary, in the first place, to study as closely as possible the phenomena themselves. We should state, however, at once, that, with but few exceptions, we have discovered nothing important that enables us to become better acquainted with the phenomena.

The volumes of theories as to the cause of this disease are altogether out of proportion to the clinical material that they provide.

In fact the nosology of beri-beri, if you wish to make it anything more than an enlarged symptomatology, is impossible, unless you have a guide to enable you to find your way in the labyrinth of symptoms. This cannot be obtained until the symptoms are more exactly described.

To the German doctors resident in Japan much credit is due, for being the first to give to clinical medicine a systematic symptomatology. If some of them, Wernich for instance, have, in our opinion, failed to obtain very definite results, if they have gone astray in taking œdema as their point of departure, they have nevertheless greatly increased our symptomatological knowledge. On the other hand, Baelz and Scheube, who took as their basis disorders of movement, have gone much further. The regular application of their mode of observation led them to believe, even for clinical reasons, that the symptoms of beri-beri could not, and ought not to, depend on anything but a multiple peripheral neuritis, the existence of which they proved by anatomical examination. The result of their labours is very

important. To Scheube is due the credit of suggesting electricity as a test of the proof of the neural nature of the disease.

Before we left for the East, we learnt what we could concerning the definition of beri-beri; we believed that there was only one disease to deal with, although it passed under different names, and we were convinced that a regular study of the pathological modifications of the peripheral nervous systems of our patients ought to be our point of departure.

# CHAPTER II.

## BERI-BERI DOES NOT DEPEND ON ANÆMIA.

We stated, at the end of the preceding chapter, that one ought not to commence the clinical study of beri-beri with the belief that it depends directly or indirectly on disorders of the vascular system. We further expressed the opinion that in considering œdema as the salient point in beri-beri, one would risk going astray. Our task then should be, in the first place, to show why we cannot agree with the view which up to the present Wernich has taken as to the question of beri-beri. Wernich, in 1877, described, for the first time, in an exact manner, the disease known in Japan under the name of kakké. Former descriptions (see Scheube) certainly have considerable historical value, but being of no further importance are passed over in silence. Van Meedervoort, after a short investigation, promptly declared kakké and beri-beri to be identical; the œdema in the lower extremities and dropsy of the serous cavities that he found in a large number, if not in all cases of this disease, led him to submit the organs of circulation to careful examination.

Numerous sphygmographic tracings, which he gives *in extenso*, leave no doubt that, during the course of the disease, the tension of the arterial system does not undergo a merely temporary lowering, to be restored when the symptoms of beri-beri disappeared. No other conclusion, however, can be drawn from this fact, which is not altogether so very unusual in a chronic disease.

On microscopical examination of the blood, Van Meedervoort finds that in beri-beri the red corpuscles do not form rouleaux. In addition, the corpuscles, in many instances, present spinous margins; and intermingled with these are seen a certain

number of faintly coloured minute bodies of new formation. Finally, one meets with large, peculiarly brilliant masses, the anatomical and physiological signification of which is not clearly defined.

Wernich, from these modifications of blood, draws the conclusion that they are owing to some obscure error of nutrition. He believes he can thus explain, on the one hand, the dropsical symptoms and the changes in the activity of the heart, and on the other, the nervous phenomena, which by the way have by no means escaped him. A secondary affection (dropsical) of the central organ is, according to him, the primary cause of the paralysis, the lack of sensation, &c., that beri-beri presents.

Beri-beri would, therefore, from Wernich's showing, partake of the nature of pernicious anæmia. But there are many grave objections to be made against his theory, although many observers have followed him.

In the first place, the alleged changes in the blood of those suffering from beri-beri, described by Van Meedervoort, and upheld by Wernich, do not occur—at least not to the extent that he makes out. From the numerous specimens of blood that we have examined in our bacteriological researches, and examined too with the necessary precautions, we conclude that the blood corpuscles of those suffering from beri-beri are generally arranged in rouleaux. One does not notice more spinous-edged forms than are always found in blood which is allowed to dry rapidly. The presence of supposed "microcytes" has no pathological signification. The large brilliant masses that we found, were composed simply of agglomerations of blood corpuscles; and although we do not wish to deny that sometimes anæmia or poikilocytosis was present, there were a great number of cases where it was not so.

In order to make more certain as to this, we asked Eykman to count the blood corpuscles of those suffering from beri-beri, and to fix the proportion of hæmoglobin contained. We give a table (see page 11), setting forth the results of these researches. The red corpuscles have been counted by means of Malassez's apparatus; the proportion of hæmoglobin has been determined by Hayem's picro-carmine method.

| NAMES. | Europeans. | Natives. | No. of red blood corpuscles. | Proportion of Hæmoglobin. | No. of days the patient has presented decided symptoms of Beri-beri. | REMARKS. |
|---|---|---|---|---|---|---|
| 1. Eykmann | E | | 6,200,000 | 10 | not ill | Dr E. considered the blood to be normal. |
| 2. Romney | E | | 6,220,000 | 10 | not ill | |
| 3. Kasare | | N | 6,250,000 | 10 | not ill | |
| 1. Pabee | E | | 6,972,000 | 10 | 45 days | |
| 2. Rekermann | E | | | 10 | 14 days | |
| 3. Kamming | E | | 7,200,000 | 10 | 100 days | |
| 4. Ranken | E | | 4,570,000 | 9 | 44 days | |
| 5. Zeydel | E | | 4,400,000 | 6 | 18 days | |
| 6. Samidinin | | N | 5,700,000 | 10 | 45 days | |
| 7. Sariman | | N | 5,600,000 | 10 | 14 days | |
| 8. Baddoeng | | N | 5,840,000 | 10 | | The blood was examined just before the death of the patient. |
| 9. Midin | | N | 5,800,000 | | 16 days | |
| 10. Towikroms | | N | 5,000,000 | 9 | 30 days | |
| 11. Sippa | | N | 5,200,000 | 8 | 11 days | |
| 12. Ramidjo | | N | 5,040,000 | 7.5 | 16 days | |
| 13. Minem | | N (female) | 5,000,000 | 8 | 42 days | |
| 14. Sardie | | N | 4,000,000 | 8 | 10 days | |
| 15. Wongsositenko | | N | 4,000,000 | 8 | 11 days | |
| 16. Kalam | | N | 5,600,000 | 10 | 16 days | |
| 17. Kalio | | N | 4,800,000 | 9 | 40 days | |
| 18. Pa Parinsan | | N | 4,000,000 | 5.5 | 15 days | |

Seeing the results of this examination, there will no longer remain any doubt as to the correctness of our statement, that in beri-beri we can have very marked anæmia, but that anæmia is by no means a constant symptom of beri-beri. Some other observers (Scheube and Baelz) had already formed this opinion on clinical grounds alone, without examining the blood.

But even had we found that beri-beri was always anæmic, as it often becomes when the disease has lasted a long time, we should not have been able to agree with Wernich. Before we can pronounce the nervous symptoms as proceeding from the exudation of serum into the subcutaneous tissues, the muscles, or the spinal cord, it is necessary to ask whether the dropsical symptoms precede those which are found in the nervous system; whether the disturbances of movement and sensibility precede the effusion, or *vice versa*. The recognised fact that some atrophic forms end almost without œdema, or even without œdema at all, is unfavourable to this opinion; on the other hand, disturbances of the nervous system, more especially of voluntary movements, are constantly present. These generally precede œdema; at least, one never finds diffuse anasarca, or dropsy of the serous membranes, without the nervous troubles of which we have just spoken being present.

The supposition of Wernich cannot, however, be true, as when progressive anæmia occurs in Europeans, as in scurvy for example, on making a thorough search, some nervous symptoms similar to those met with in beri-beri would no doubt be found. On Wernich's supposition it would be as correct to count scurvy as a disease of the nervous system, because it exhibits some nervous disturbances, as it is to place beri-beri amongst the blood diseases, because it happens to exhibit some secondary vascular phenomena. In beri-beri, nervous disturbances are present from the commencement; and if, after the observations of Scheube and Baelz, he continue to defend his opinion, it would mean that he had not paid attention to the initial symptoms of beri-beri.

Wernich contends that it is not sufficient to merely demonstrate the anatomical degeneracy of the peripheral nerves. In

several other long-standing diseases,[1] such as infectious fevers, locomotor ataxy and marasmus, similar modifications of the peripheral nerves are met with; it therefore no longer suffices (and in this we share Wernich's opinion) to merely ascertain anatomically the degeneracy of the nerves.

Without wishing to diminish in the least what we owe to Baelz and Scheube for our knowledge of beri-beri, we must say that this is the weakest point of their contention.

So long as the initial symptoms of beri-beri had not been examined by means of electricity, so long as one had not shown that there are, from the commencement, clinical disorders of the motor nervous system peculiar to the peripheral paralysis of beri-beri, the verification of the degeneration of the nerves by post-mortem examination was no doubt an important matter. But it is not conclusive as to the nature of the primary lesion.

We will return to the consideration of this subject by-and-by. We cannot therefore adopt Wernich's contention, because neither clinically nor anatomically has he constantly found anæmia to be present; nor can we on the other hand follow those who have studied beri-beri by taking œdema as their point of departure. We will only note in passing, that the opinion of van Leent, according to which one would always find albumen in the urine, and sometimes even a great deal, is not in accordance with our observations. Albuminuria may well exist as a complication, but close examination will not justify us in regarding beri-beri as a disease of the kidney.

[1] Pitres et Vaillard. Contribution à l'étude des névrites périphériques survenant dans le cours ou la reconvalescence de la fièvre typhoïde. Revue de méd. 1885, p. 985.

*Ibidem.* Des névrites périphériques chez les tuberculeux. Revue de méd., 1886, p. 193.

Lissauer. Beiträge zum Faserverlauf im Hinterhorn des Rückenmarkes, etc., Arch. f. Psych., vol. xvii., fasc. 2.

Dejerine. Des altérations des nerfs cutanés chez les ataxiques, etc. Arch. de physiol., 1883, p. 72.

*Ibidem.* De la variabilité des névrites cutanées des tabétiques. Compt. rend. de la Soc. de Biol., 1884, p. 405.

Oppenheim et Siemerling. Beiträge zur Pathologie der Tabes dorsalis und der peripherischen Nervenkrankeit. Arch. f. Psych., vol. xviii., pp. 98 and 487.

# CHAPTER III.

## THE INITIAL PHASE OF BERI-BERI.

No disease presents so many diverse symptoms as beri-beri. This is the opinion of all authors, and their statements are not without reason.

Wernich, on the one hand, describes the variety "destructive kakké," as ending fatally in a few hours or days; on the other, some subacute forms of short duration ending in recovery; and yet again he gives details of some cases of beri-beri of a chronic nature, where those who were affected lived many years.

We must consider first the subacute form of beri-beri.

Upon our arrival in the Indies, some trustworthy persons spoke to us of these "destructive cases." They told us how soldiers, who had mounted guard in perfect health, had died in a few hours, victims of this terrible disease. We very soon satisfied ourselves as to this. We arrived at Atjeh on the 19th February 1887, and naturally took a lively interest in the health of the soldiers of the Madoura native militia, who had been stationed at Atjeh since the 12th of January of that year.

These troops came from the island of Madoura, situated to the north-east of Java, where beri-beri was not prevalent. In number 340, they were not the well-nourished troops one would have wished to have seen at Atjeh; on the contrary, they were sickly, badly nourished men, who, in consequence of diverse circumstances, found themselves at Atjeh under very unfavourable conditions.

When we arrived, none of these militiamen were apparently ill. However, in the last week of February, 11 men had to be sent away, and 1 died of beri-beri. In the following week, 75 men had to be sent elsewhere, and 14 others had succumbed to beri-beri, chiefly of the subacute form. A week later all those who

remained were sent back to their homes. It is a fact that several soldiers, who in the morning were firing at the target, and shooting well, even making bull's eyes, were dead at night. Three cases of the "destructive" form were on one occasion noted in a single day.

How is it that these militiamen, who arrived at Atjeh when beri-beri was very prevalent, did not get the disease during the first five weeks of their stay?

This record is quite consistent with the facts communicated by some other authors. Hoffmann says that strangers do not take the disease until the second year; Christie, Hunter and Aitken state that it develops only after a stay of from eight to ten months in a place where beri-beri prevails.

It was suggested that the fact of the native Java militiamen falling ill at the end of five weeks, was owing perhaps to the violence with which the disease raged at Atjeh. Sugenoja states that he had never seen it spread so rapidly or with such violence in Japan.

The explanation of this fact which appears to us the most admissible, is that, through imperfect observation, we were unacquainted with the initial symptoms of beri-beri. It would otherwise be incomprehensible that the disease had spared these soldiers for five weeks, to afterwards attack almost all of them in the short period described. The most natural explanation would be that they were infected by beri-beri on their arrival, but that the affection did not declare itself in a visible manner until the end of five weeks. In fact, amongst the men supposed to be well, who were sent away from Atjeh in the first fortnight of March, Dr Huysman, who inspected them at Olehleh before they left, found few of them who did not already present one of the symptoms of beri-beri, namely, slight œdema along the crest of the tibia. All the men we examined were ill. It is therefore most likely that they were suffering from premonitory symptoms, an initial phase, in fact, which was obscure, and but ill-understood. To elucidate this point, we asked that all those whom the doctors suspected of shamming (and the doctors at Atjeh had truly acquired a sufficiently large experience in a matter of this sort), should be sent to us for examination.

The symptoms the military surgeons regarded as indicating beri-beri at that time were as follows: Slight œdema along

the crest of the tibia; a puffy, pasty face; difficulty in certain movements, observable only at first when the patient walks quickly or attempts to go up stairs; some paræsthesia or anæsthesia of the lower extremities; palpitation of the heart; a slightly quickened pulse, or rather a pulse which remains within normal limits whilst the patient is at rest, but which upon the least movement goes up to 90 or 100 beats per minute; a slight increase of dulness of the heart's area to the right; a marked contrast between the violent impulse of the heart and the small and feeble pulse; a prolonged first and a reduplicated second sound of the heart. These symptoms form a complete summary of knowledge of the symptoms of beri-beri in the early stage.

The sad experience that one acquired, with regard to very severe cases, was the reason that the presence of one of these symptoms was sufficient to establish a suspicion, if not a diagnosis, of the commencement of beri-beri. With the exception of some slight anæsthesia, of which we will speak presently, as a rule hardly any of the soldiers sent to us for examination presented symptoms of the nature mentioned above. What we had seen at Batavia, however, taught us the great value of electrical examination. We already knew from experience that in beri-beri the visible disorders of motion do not always agree with the results obtained by examination of the electrical reaction of the muscles and nerves. As we must treat this subject more in detail further on, we will only say here, that almost all those suspected of shamming presented some, and at times very strongly marked,[1] deviation from the normal.

[1] We will here give some idea of the apparatus we made use of in our experiments :—We had a Hirschmann's resistance coil registering up to 5000 Siemens units, also one of his induction batteries provided with a soft iron cylinder. When this cylinder was removed, and the secondary coil withdrawn as far as possible from within the primary, the strength of the current, as indicated by the scale reading, was zero. If now the secondary coil was slid right in again, without, however, having its iron cylinder inserted, the coil must altogether have moved through a distance of 100 mm., and the strength of the current, as indicated by the scale reading, was 100; and finally, if the iron cylinder, which was 140 mms. in length, was now introduced into the secondary coil, the current reached its maximum value, or 100+140. During these experiments we were careful to maintain the primary current as constant as possible, by means of frequently renewing the Leclanché elements employed. We had also one of Hirschmann's absolute galvanometers of the vertical type, but the registrations of this were never quite correct, more particularly after our arrival in the East—they were always too high. MM. van der Stok and Figée, Director and Vice-Director of the Batavian Observatory, kindly lent us their aid in the management of this instrument. The particular placing of the instrument only rendered its control possible by

We have tabulated our observations (see page 18). Although this is not the place to go into the details of the results obtained, there is one important conclusion which strikes one promptly, viz., that there are, with regard to quantity as well as quality,

means of Thomson's dial electrometer, in the position 1—1. The electrometer received a current from 12 Latimer Clark's elements.

1 Lat. Clark = 1.435 volts,
consequently 12 Lat. Clark = 17.22 volts,
which gives a deviation of 52.5 mms.
1 mm. = 0.328 volts.

For W. one found by the galvanometer 489 ohms.

| W. in ohms. | Deviation in mm. | Volts. | Calculated in Milliampères. | Milliampères registered. | Difference. |
|---|---|---|---|---|---|
| 30489 | 13.7 | 44.94 | $\frac{44.94}{30489.1000} = 1.4746$ | 1.5 | +0.03 |
| 25489 | 13.0 | 42.64 | $\frac{42.64}{25489.1000} = 1.6729$ | 2.0 | +0.33 |
| 4168 | 27.8 | 9.12 | $\frac{9.12}{4168.1000} = 2.1881$ | 2.5 | +0.42 |
| 5206 | 37.2 | 12.20 | $\frac{12.20}{5206.1000} = 2.3435$ | 2.8 | +0.5 |
| 4168 | 35.0 | 11.48 | $\frac{11.48}{4168.1000} = 2.7543$ | 3.6 | +0.8 |
| 15489 | 126.5 | 41.56 | $\frac{41.56}{15489.1000} = 2.6832$ | 3.5 | +0.8 |

As the combination 4 has clearly indicated four times more than 1—1, the proportion per cent. of difference remains the same. But as we are obliged to give up absolute values, relative ones are sufficiently satisfying for our object. The control of absolute value is, however, necessary. For practical reasons we have nowhere applied corrections.

The following are the abbreviations which we make use of :—

| | |
|---|---|
| Min. Ka. Sc. | = Contraction of muscles at the Kathode on the closure of the most feeble current. |
| Min. An. Sc. | = Contraction of muscles at the Anode, on the closure of the most feeble current. |
| Ka. Sc. | = Contraction at the Kathode at the closure of the current. |
| An. Sc. | = Contraction at the Anode at the closure of the current. |
| Ka. Oc. | = Contraction at the Kathode at the opening of the current. |
| An. Oc. | = Contraction at the Anode at the opening of the current. |
| cc'c''CC'C'' | = In proportion as the contraction increases in strength, it is so marked. |
| Ka. DT, An. DT, | = Constant tetanus presenting itself, either by Kathode or Anode, after closure of current. |
| mA. | = Milliampère. |
| $\omega$ | = Slowness of contraction. |

Unless expressly stated to the contrary, the surface of the different electrodes is always 10 centimetres square.

TABLE OF PERSONS SUSPECTED OF SHAMMING BERI-BERI, AND RECOGNISED AS REALLY SUFFERING FROM THE DISEASE BY MEANS OF VARIATIONS IN THE ELECTRICAL REACTION OF THE MUSCLES SUPPLIED BY THE EXTERNAL POPLITEAL NERVE.

| NAMES. | | Indirect irritability (minimum contraction) of the anterior tibial muscle (external popliteal nerve). | | | | Direct irritability of the anterior tibial muscle. | | | | Resistance. | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | On the Right Nerve. | | On the Left Nerve. | | On the Right. | | On the Left. | | | |
| | | Continuous Current. | Induced Current. | Continuous Current. | Induced Current. | Continuous Current. | Induced Current. | Continuous Current. | Induced Current. | On the Right. | On the Left. |
| 1. Stavast | E | 10 mA | | | | 20 mA Ka Sc = An Sc∞ | | | | 1150 | |
| 2. Van der Seppe | E | 10 mA | | | | 8 mA An Sc Ka Sc∞ | 100+26 | | | 2900 | |
| 3. Boon | E | 8 mA | | 10 mA | | 20 mA Ka Sc = An Sc | 100+38 | 19 mA | 100+36 | 1400 | 1150 |
| 4. Loos | E | 7 mA | | 10 mA | | 11 mA Ka Sc∞ 13 mA An Sc∞ | | 14 mA Ka Sc = An Sc∞ | | 1150 | 1150 |
| 5. Ratman | E | 5 mA 14 mA Ka Dt | 50 | 6 mA 17 mA ta Dt | 46 | 6 mA Ka Sc | | 8 mA Ka Sc | | 2900 | 2900 |
| 6. Sotaraem | N | 5 mA 20 mA Ka Dt | 70 | 4 mA 17 mA Ka Dt | 50 | 12 mA | | 13 mA | | 2050 | 1700 |
| 7. Nagasio | N | 8 mA Ka Sc | 85 | 7 mA | 95 | 15 mA | 100+40 | 16 mA | 100+56 | 2050 | 2450 |
| 8. Sokrones | N | 8 mA | | 7 mA | | 16 mA | 90 | 15 mA | 86 | 2050 | 2050 |
| 9. Kromodimedjo | N | 6 mA | 55 | 6 mA | 57 | 14 mA | 100+40 | 19 mA | 100+32 | | |
| 10. Setrodomo | N | | | | | 720 mA Ka Sc = An Sc∞ | | | | | |
| 11. Saman | N | 3 mA Ka Sc 12 mA Ka Dt | 45 | 4 mA Ka Sc 17 mA Ka Dt | 30 | 6 mA | 68 | 7 mA | 78 | 3400 | 2900 |
| 12. Royodongso | N | 6 mA 720 mA Ka Dt | 26 | 2 mA 16 mA Ka Dt | 28 | 9 mA Ka Sc∞ | 60 | 8 mA | 60 | 2050 | 2450 |
| 13. Pakartama | N | 14 mA 15 mA Ka Dt | 30 | 4 mA 16 mA Ka Dt | 30 | 9 mA Ka Sc∞ | 42 | 10 mA Ka Sc∞ | 50 | 2900 | 2900 |
| 14. Singo | N | 3 mA 12 mA Ka Dt | 25 | 3 mA 9 mA Ka Dt | 36 | 8 mA | 40 | 6 mA | 50 | 2900 | [2]2900 |

REMARKS.

1. The minimum force of the current is generally given in milliampères, by which a Ka Sc is produced by an electrode of 10 centimetres square. If An Sc is greater or equal to Ka Sc it is shown. When a decidedly slow contraction is observed it is thus noted ∞. Resistance is not indicated in ohms, but in Siemens units.

2. After having been examined, this patient declared that he was not suffering from beri-beri, but really wished to go to Padang. Ten days later, however, he returned to hospital with his legs swollen.

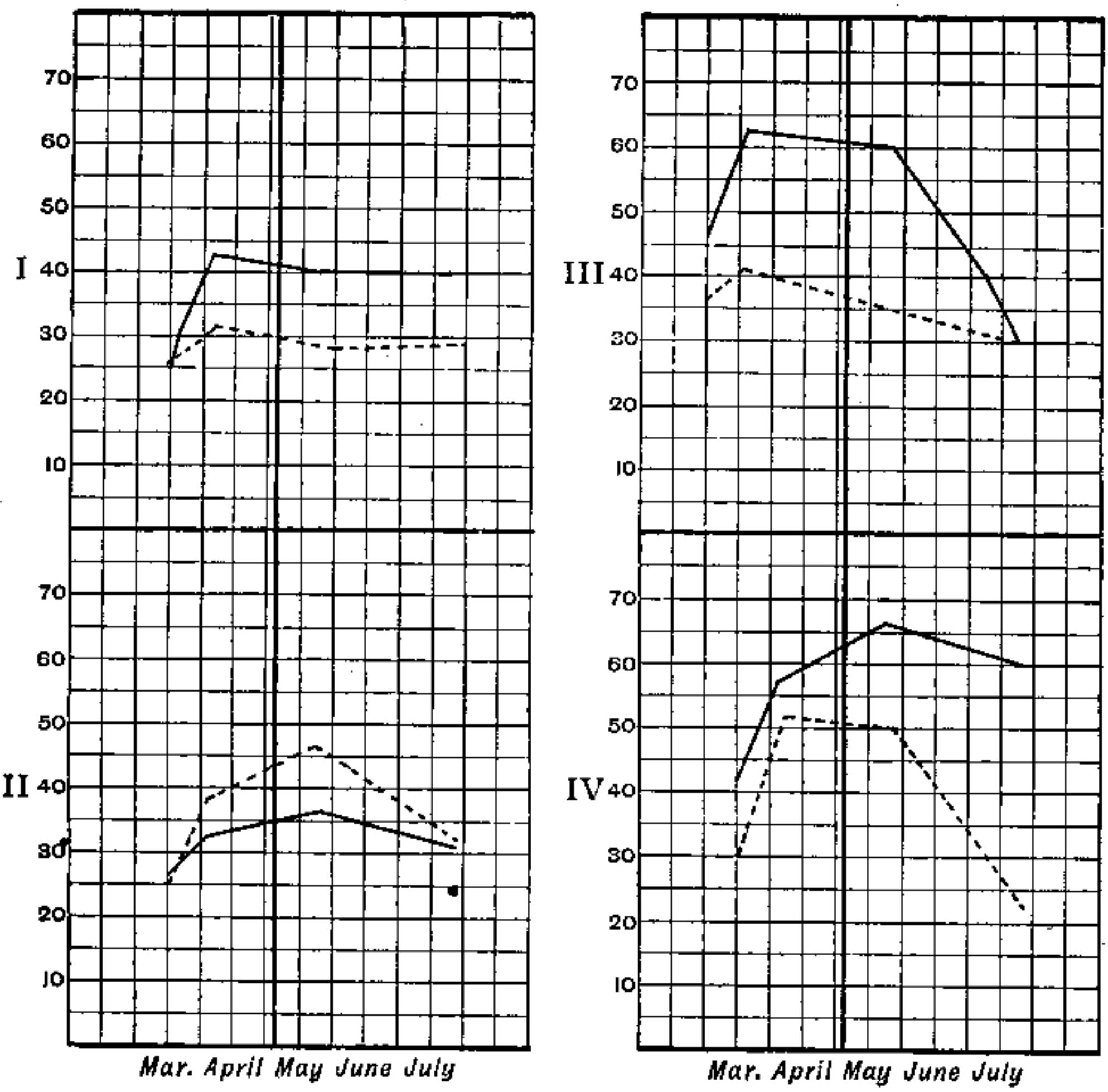
some important variations in the muscular and nervous reactions, which, if they cannot all be ranked in the reaction of degeneration, can nevertheless, taking the words in their widest signification, almost invariably be so classed. The table was obtained as the result of contractions which are produced from the feeblest currents.

In the absence of signs or symptoms, when even the patient himself feels scarcely indisposed, frequently long before he finds any difficulty in walking, often also before he has any distinct symptoms of œdema, it is possible to diagnose beri-beri by electricity. This is an important fact, the basis of our opinion concerning the clinical classification of the disease. Electrical variations are, however, not the only symptoms of this phase of the disease.

In our later researches we took as a point of departure an observation of Wernich's that we were fully able to confirm. When beri-beri is well developed, one always finds somewhere in the calf of the leg a space, generally very circumscribed, where susceptibility to feeling no longer exists to a light touch.

We were also greatly astonished by Wernich's statement, that the tactile areas had but little if at all diminished, because we had carefully noted amongst the first symptoms of beri-beri an augmentation of the diameter of these tactile areas. It was as much so among the men who had been supposed to be shamming as among ourselves. There was hardly any one at Atjeh who, after passing some months there, did not complain of a certain numbness of the legs. Two of the members of our commission never complained of this feeling, but the other two complained greatly. One of the two so afflicted noticed a slight œdema along the crest of the tibia; the other complained of pain and weight in the legs, and of palpitations such as he had never experienced before.

We give a chart showing how, as far as we four were concerned, from the commencement of our stay at Atjeh, the tactile zones became larger. The vertical black lines which cut the charts in two show when we left Atjeh. The sketches themselves show at once in millimetres the diameters of the tactile zones.




This initial phase of beri-beri is characterised by quantitative alterations, consisting of a diminution of irritability generally, for the two kinds of currents; very often also there is to be made out some qualitative modifications of the electrical reactions of the dorsal muscles of the foot; this phase, characterised further by an augmentation of the diameter of the tactile zones at a fixed spot in the leg, has not been observed by any previous authors. It was not possible they could perceive it, because the most striking symptoms could only be distinguished by the aid of a galvanometer, which they had

# CHAPTER IV.

## SUBACUTE BERI-BERI.

### DA SYLVA LIMA'S MIXED FORM—THE DROPSICAL ATROPHIC SUBACUTE FORM OF SCHEUBE.

When in the preceding chapter we drew attention so prominently to the two most salient symptoms, we by no means wished it to be inferred that other symptoms were not present in the initial phase.

One generally finds at this stage a slight œdema along the crest of the tibia; sometimes even a slight increase in area of the right side of the heart is capable of demonstration. But in order that our description may proceed systematically, it seems better, before studying the signification of these symptoms, to regard beri-beri in all its stages of development. With this end in view, we choose, in the first place, some cases of subacute beri-beri, which present the two series of symptoms peculiar to this disease. We believe, with Baelz and Scheube, that these two series of phenomena depend upon a degeneration of the peripheral nerves.

We divide provisionally these phenomena into those which are connected with the organs of circulation, and those which depend upon the degeneration of the sensory nerves and of the nerves connected with the voluntary muscles. It is only by such means that we can show the transition from the initial phase of beri-beri to the completely developed disease.

In introducing this initial phase we hope to re-establish a certain amount of harmony amongst the apparently wide differences of opinion of the various authors. Opinions are greatly divided on the question as to whether or not beri-beri commences with fever. The fact is that beri-beri always commences slowly and without fever; but in a later stage it

may rather suddenly happen that an increase in the symptoms of the disease is accompanied by fever.

Beri-beri is a disease which cannot prove fatal in a few hours; but in a later stage, an exacerbation of the disease may prove rapidly fatal, by a sudden affection of the cardiac nerves, causing an acute paralysis of this organ, or perhaps dropsical complications. Beri-beri is never ushered in by cramp; but an acute exacerbation, affecting a large number of nerves of motion, is often accompanied by phenomena of irritation in the muscles of the legs, and may produce so-called "convulsive beri-beri," so well described by Overbeck de Meyer. It never happens at the commencement of the disease that the patient suffers any violent paræsthesia; but at a later stage, an acute exacerbation of illness may be accompanied by phenomena of irritation in the nerves of sensation, and cause that terrible agony known under the name of "painful anæsthesia." The patient is prostrated by an agonising tingling in the upper and lower limbs, set up by the least excitement of a cutaneous nerve.

But before describing these exacerbations in greater detail, it will be useful to follow the clinical history of a case of the most common variety, the subacute or dropsical atrophic form.

Case I.—Mang, aged, as we estimated, about 21 years, born at Batavia, served for five years as a sailor on board the *Hydrograaf*, near the island of Ourust. There were several persons suffering from beri-beri on board this ship. He had never been ill before. According to his own statement, which we proved to be correct, he fell ill on the 4th of December 1887. His legs became swollen a few days afterwards; he experienced an unbearable formication in the hands and feet; but what he suffered from most was a sharp pain in the calves. He described his sensations as an intense pain in the bone. At the same time the movements, more especially walking, became difficult. On the 13th of December he entered the hospital at Batavia. The swelling of the legs diminished rapidly, but the paræsthesia lasted several days longer. The intense pain disappeared when he remained quiet, but reappeared when he walked. He was not entirely paralysed, nor had he ever been, but his gait was tottering. The patient said that he had never had fever, nor any

difficulty in making water or relieving his bowels; he ate, drank, and slept well.

*State when seen on the 31st of December.*—The patient is strongly built and very muscular. He has no appearance of suffering. No anæmia or cyanosis of the visible mucous surfaces. He interests himself in his surroundings, and relates with vivacity his state since the commencement of his illness. The rate of the pulse is 94 to the minute; but it rises to 116 on the slightest bodily exertion. The pulse is moderately tense, being neither violent nor bounding; the type of respiration is abdominal, and 26 to the minute; the heart's impulse is pronounced, and in the mammillary line at the fifth intercostal space.

The dulness of the heart's area goes beyond the left sternal edge, but does not reach the middle of the sternum. The cardiac sounds are sonorous and pure, but there is reduplication of the second sound, and the pulmonary diastolic sound is augmented. Otherwise there is nothing abnormal in the organs of the thorax and abdomen. The patient's face is a little puffy, and looks pasty, but pressure with the finger leaves no impression. Pressure of the finger leaves a hollow on the inner surface of the tibia, but there is no œdema at the ankle. The pupils react rapidly and correctly, as well to a direct as a side light. The higher senses are intact: he sees well, hears the tick of a watch at a considerable distance, and can readily distinguish salt from sugar.

*The condition of the muscles.*—The muscles all over the body are well developed, and firm to the touch; some, for example the muscles of the calf, are very sensitive to pressure, and seem to have become more resistant. On their contraction they bulge to such an extent that they present the appearance of a circumscribed swelling. When struck by means of a percussion hammer they are not irritable; nor is there any idio-muscular contraction present. The majority of the movements can be made actively and passively. Nevertheless, when the patient is lying down, it is impossible for him to flex his foot, and the extension movements can easily be arrested. The flexion movements at the knee are readily made; very slight resistance, however, suffices to stop the extension of the leg. Adduction, abduction, and flexion of the thigh are easily made; it is in flexion that the greatest resistance has to be overcome. The dynamo-

meter registers in the right and left hands 27, at the elbow 25. If the patient gets up, one notices some considerable difficulty in walking. He raises his foot from the floor with difficulty, lifts it high and puts it down as if it were pushed forward. The patient cannot stand on one foot, nor stand on tiptoe. If he wishes to squat on the floor, he does it very awkwardly, and threatens to fall. While he is lying down he is able to bend and stretch his body, and to move his upper extremities freely, as well as the eyes and the muscles of his face and tongue. He staggers when standing with his eyes closed. One cannot, however, record any distinct defects of co-ordination; whilst recumbent and with his eyes closed, he can approach slowly but correctly the heel of one of his legs towards the knee of the other. The motor nerves are not rendered irritable by mechanical means.

| INDUCED CURRENT— | Right. | Left. |
|---|---|---|
| Nerve. External Popliteal, . . . . | not irritable. | |
| ,, Internal Popliteal, . . . . | | |
| Muscle. Tibialis Anticus, . . . . | | |
| ,, Extensor Communis Digitorum, . . | | |
| ,, Extensor Proprius Pollicis, . . . | | |

| CONTINUOUS CURRENT— | | Right. | Left. |
|---|---|---|---|
| Nerve. External Popliteal, | min. Ka. Sc. | 10 m A. | 8 m A. |
| | min. An. Sc. | 12 m A. | 9 m A. |
| | min. An. Oc. | 12 m A. | 10 m A. |
| Muscle. Tibialis Anticus, | min. Ka. Sc. = min. An. Sc. | 14 m A. | 12 m A. |
| ,, Ext. Proprius Pollicis, | min. Ka. Sc. = min. An. Sc. | 16 m A. | 14 m A. |

The contractions of the muscles are a little sluggish and rather feeble.

*The sense of touch.*—All over the body any rough touch is felt, but when the patient's eyes are closed, and one touches him with a feather without asking him any questions, only asking him to state when he felt anything, he would give a confused account of some indefinite sensation. In the middle of the calf, a light touch with a feather is not felt, but a more rough application, such as by a strong quill, more especially when it is moved backwards and forwards, is recognised. As the quill is passed downwards from the back of the knee towards the heel, one

notices a great diminution in the rapidity of the transmission. This anæsthetic area spreads over the posterior surface of the [illegible] as far as the tendo Achillis. In the hand also, over the thenar and the hypothenar eminences, it frequently happens that the touch of the quill is not felt, whereas at the finger ends it is appreciated readily. Along the back, on the chest, and on the face, the least touch is felt.

DIAMETER OF THE TACTILE ZONES.

| | Right. | Left. |
|---|---|---|
| Index finger, . . . . . | 2 mm. | 2 mm. |
| Palm of the hand, . . . . | 20 ,, | 20 ,, |
| Chest, . . . . . | 30 ,, | 25 ,, |
| Along the calf, . . . . | 100 ,, | 75 ,, |

The patient localises well. He readily recognises what part of his body is touched. *The feeling of pain* is quite intact. Pricking and pinching are always painful. A tube containing water heated to 50° C. is recognised as hot to the touch, except upon anæsthetic areas. A tube filled with melting ice elicits the sensation of cold everywhere. It is remarkable that the patient says that the hot tube feels cold when applied to the calf. The patient's muscular sense is intact, and he can imitate with one leg all the movements that are passively made for him with the other. Some nerves, especially the anterior crural, are very painful when touched; a hyperalgesia of the skin, which almost corresponds to the superficial ramifications of this nerve, would appear to depend upon it.

Abdominal and scrotal reflexes are, on the other hand, readily excited. Westphal's symptom (also in conformity with Jendrassik's method) is present. One could not succeed in producing any reflex movements by tickling the soles of the feet.

The patient has no fever. The temperature this morning was 37.2°, and in the evening 37.6°. Nothing indicated that his life was in danger. He remained in the same state until the 2nd of January, but during the night between the 2nd and 3rd of January, he began to vomit, and died in a few hours. In the report on the autopsy we find among other things, 100 grammes of a pale yellow serous fluid in the pericardium, enormous dilatation of the right heart, and hypertrophy more especially of the wall

We have given this case in detail, although omitting the electrical phenomena in a great number of the nerves and muscles, because we believe it exemplifies a certain type which is often met with in beri-beri.

We would first call attention to the electric reaction of the muscles which are controlled by the external popliteal nerve, and that of the nerve itself, because it is exactly this form of reaction of partial degeneration which is so frequently met with in beri-beri. The suppression of irritability to the Faradic current, whether applied directly or indirectly to these muscles, is complete. There is at the same time a considerable diminution of the indirect muscular irritability to the galvanic current, and a still greater diminution of its direct irritability.

In addition to this a contraction, more or less slow, which appears when the current is uniform, at the closing as well of the anode as of the kathode, characterises the deviation as qualitative.[1] It is evident therefore that in beri-beri we have a special form of the reaction of partial degeneration. That which is especially peculiar is the considerable amount of diminution of the irritability of the muscle to the galvanic current. In the case of a patient who said he was quite well four weeks before, and who since then had only noticed disorders in movement, this diminution of irritability to the galvanic current was well marked when as yet the patient felt nothing.

Whoever has observed a complete peripheral facial paralysis knows that, in the first weeks of its existence, an augmentation and not a diminution of the irritability of the muscle is present. In beri-beri, with an almost complete analogy to paralysis, how is it that a totally different condition of things is met with? To clear up this matter, one can imagine our desire to examine patients during the acute phase. We set about this by requesting that all those suffering from acute beri-beri should be sent to us, and here we present shortly the two following cases.

Case II.—D., a European, aged 36, has been residing at Atjeh for one year. On April the 20th he entered the Panteh-Perak Hospital, for a slight wound on the foot. A few

[1] Where not otherwise stated, the surface of the different electrodes is 10 centimetres square.

days after his arrival he had an attack of vertigo, and complained of headache, especially on the right side. To these symptoms were added diarrhœa, accompanied by nausea, as many as eight stools a day being passed. On the evening of April the 25th we noticed, for the first time, an elevation of the temperature up to 38.4°, and from that date he had fever up to May the 4th. The fever had a remittent character, with oscillations between 38.4° as a minimum, and 39.7° as a maximum. On May the 4th the evening temperature had fallen to 37.4°. We examined him on the 26th of April, that is, one day after a marked elevation in temperature had been noticed, and under the supposition that the patient had caught beri-beri in its acute stage in the hospital. The actual state was as follows:— The patient complains of pains in the head, especially on the right side. All the points of exit of the right fifth cranial nerve on the face are painful; the radial, ulnar, crural and peroneal nerves are, especially on the right, very tender when pressed; this is not the case with the median nerve. A very slight œdema along the inner surface of the tibia can be made out, but it does not extend to the ankle. In the legs, sensibility to touch is lessened to light contact, such as stroking with a feather; on both sides along the posterior surfaces of the calves of the legs and on the dorsum of the foot there are some spots altogether anæsthetic. At these places tubes containing cold and hot water respectively could not be distinguished the one from the other. All the reflexes exist. The pupils are of equal size and react well. The pulse is large, soft, bounding, 96 per minute, rising after bodily exertion to 112. The heart's impulse is increased, but normal in position; the præcordial dulness is within its normal limits, and the heart's sounds are pure. Respiration is of the costo-abdominal type, 24 per minute. The organs of the thorax and the abdomen are in their normal state, except that there is a slight fulness of the spleen, so common in the tropics. Walking is a little difficult, and he cannot hop on his right foot. In walking quickly he seems to have increased difficulty in moving the right leg. Otherwise, he can execute all motions actively when there is no resistance offered. The muscles of the calf are full and firm to the touch. They are

after percussion, but no fibrillar contraction is evident. The electrical reactions are as follows:—

INDUCED CURRENT.

| | Right. | Left. |
|---|---|---|
| N. External Popliteal branch to the Tibialis Anticus, | 100 + 20 | 60 |
| N. Internal Popliteal, . . . . . | 100 + 20 | 100 + 35 |
| M. Tibialis Anticus, . . . . . | 80 | 80 |
| M. Extensor Proprius Pollicis, . . . . . | 100 + 40 | 100 + 35 |
| M. Gastrocnemius (inner head), . . . . | 100 + 40 | 100 + 50 |

All the contractions are slow, except those of the anterior tibial muscle.

CONTINUOUS CURRENT.

| Right. | | Left. | |
|---|---|---|---|
| *N. External Popliteal.* | | | |
| Min. Ka. Sc., . . . | 2¼ mA. | Min. Ka. Sc., . . . | 2½ mA. |
| Ka. DT., An. Sc., . . | 16 mA. | Ka. Sc., An. Sc., An. Oc., | 12 mA. |
| | | Ka. DT., An. SC″., An. OC., | 20 mA. |
| *N. Internal Popliteal branch to the Gastrocnemius muscle.* | | | |
| Min. Ka. Sc., . . . | 10 mA. | Min. Ka. Sc., . . . | 7 mA. |
| Ka. Sc′., min. An. Sc., . | 11 mA. | Ka. Sc′., min. An. Sc., . | 9 mA. |
| Contraction very slow. | | | |
| *M. Extensor Proprius Pollicis.* | | | |
| Min. Ka. Sc., . . . | 12 mA. | Min. Ka. Sc , . . . | 12 mA. |
| Ka. Sc., min. An. Sc., . | 17 mA. | Ka. Sc., An. Sc., . . | 14 mA. |
| An. Dc., with 30 cells, . | 20 mA. | An. Dc., with 30 cells, . | 20 mA. |
| All the contractions are extremely slow. | | | |
| *M. Tibialis Anticus.* | | | |
| Min. Ka. Sc., . . . | 6 mA. | Min. Ka. Sc., . . . | 7 mA. |
| Contractions slow. | | | |
| *M. Gastrocnemius (Inner head).* | | | |
| Min. An. Sc., . . . | 11 mA. | Min. An. Sc. = min. Ka. Sc., | 14 mA. |
| An. Sc.′, min. Ka. Sc., . | 12½ mA. | An. Sc.′, Ka. Sc.′, with 30 cells, | 20 mA. |
| Contractions excessively slow. | | | |

The patient is altogether insensible to very strongly induced currents along the calves; he is thoroughly conscious of the position of his muscles.

The patient, when able to walk again, complained of heaviness in the limbs and of palpitations; in this state he was discharged, and sent back to Atjeh.

CASE III.—C. S., a European, aged 23, is the youngest of a family of eleven, of whom three are still alive. He has had

no serious illness since infancy. On arrival in Sumatra, on the 4th of September, he was sent immediately to join his battalion at Meester-Cornelis. A careful examination showed that within twelve days afterwards he was indisposed; although he distinctly dates his sufferings only from the night of the 2nd and 3rd of December, *i.e.*, twenty days afterwards. On that night he vomited, had two or three rather loose stools, and believes he had fever. He was admitted to the Hospital at Batavia on the 4th of December, his temperature ranging as follows:—

| | Morning. | Evening. |
|---|---|---|
| 4th December, | 37.6° | 38.5° |
| 5th „ | 38.7° | 39.4° |
| 6th „ | 38.4° | 39.2° |
| 7th „ | 38.8° | 40° |

Upon the 7th of December the patient complained of pains in the calves. The doctor who treated him recorded a slight œdema on the shins, and a very great susceptibility of the muscles of the calf to pressure. The legs have become so stiff that the patient can no longer walk. Upon the 8th of December the temperature again fell, and by the 10th of December it registered 37.4°

*Clinical state on the 5th of December.*—The patient is a well-built man, with an anæmic aspect. His face is slightly puffy, and the lips somewhat cyanosed. The pupils are equal and react well. Every motion of the head, eyes, face, and tongue can be carried out. In the neck a true venous pulse is noticed: the pulsations of the jugular veins can be seen even from a distance. The pulse is small and weak, numbering in repose 64, but rising to 128 on slight exertion. The cardiac impulse is not visible when the patient is lying down. The area of præcordial dulness commences at the third intercostal space, crosses the mammillary line at the fifth space, and ends two centimetres and a half further on towards the left; over the sternum the dulness is perceptible as far as the right sternal edge. The heart's sounds are pure but very feeble, and scarcely audible when the patient is lying down. The percussion dulness between the lung and the liver reaches to the 6th rib in the right mammillary line, and descends three centimetres during inspiration. The splenic dulness commences at the ninth

rib in the left anterior axillary line. The vertical measurement of the area of dulness is eight centimetres. Beyond an undoubted effusion of serous fluid in the pericardium, there is nothing anomalous in the internal organs. The urine does not contain albumen, sp. gr. 1011, reaction acid. Walking is associated with some difficulty. The patient can stand on tip-toe, but cannot jump on his right leg; the movements of the right leg can be restrained with less force than those of the left. The dynamometer at the back of the knee only marked on the right leg 10, and the left 20, whereas in a cachectic patient in the next bed, not suffering from beri-beri, it immediately marked 35. The skin is sensitive to moderately firm contact everywhere. All the reflex movements exist. Spinal epilepsy. Reflexes: the knee reflexes, and the reflex movements caused by tickling the soles of the feet are pronounced. The diameter of the tactile area, along the inner aspect of either calf, is on the right leg 44, and on the left 24 millimetres.

Electrical Examination—

INDUCED CURRENT.

| | Right. | Left. |
|---|---|---|
| N. External Popliteal, . . . . | 100 + 5 | 92 |
| M. Tibialis Anticus, . . . . | 100 + 20 | 100 + 40 |

CONTINUOUS CURRENT.

| | | |
|---|---|---|
| N. External Popliteal, . . | min. Ka. Sc. 9 mA. | 8 mA. |
| M. Tibialis Anticus, . . | min. Ka. Sc. 14 mA. | 13 mA. |

A slow contraction takes place, both by direct and indirect irritation.

*December 10th.*—After rest in bed and treatment, the increase of præcordial dulness, which was noted towards the left, has completely disappeared, but the increase towards the right side is maintained. The first sound of the heart is prolonged, and there is a well-marked reduplication of the second. The patient has no fever, and leaves the hospital "cured."

Whatever may be the real difference between these two cases, it is evident that the symptoms presented by each are at almost total variance. The cases illustrate, however, the variety and

multiplicity of the signs and symptoms of beri-beri, and are of the greatest importance clinically. One fact, however, must be evident, viz. :—that in spite of appearances, it is impossible that muscular excitability can disappear after a single day's illness to the extent described. It must be taken for granted, that the patient had been suffering from initial symptoms, which, being slight, had been disregarded, and this *a priori* conclusion is completely borne out by a careful consideration of the clinical history. In fact the initial phase of beri-beri ends with, so to speak, an attack of fever; it is the symptom which first causes the patient to seek medical advice and so come under observation. But the disease did not commence with this attack of fever; in fact, in our first case (see Case No. I), it is probable that the patient had no ailment before becoming acutely paralysed.

It is necessary at this stage to describe as fully as possible the initial phase of beri-beri. The patient first complains of flying pains, of a feeling of weight in the limbs, and that he is quickly fatigued. In addition, one can early ascertain a certain number of variations in the electrical phenomena of the motor nervous system. They may be considered in part as partial reactions of degeneration, in part as a simple quantitative diminution of the direct and indirect irritability of the muscles for the two kinds of currents. At the same time there is often a slow contraction, which, as a qualitative variation, characterises the reaction as one of degeneration. These symptoms are accompanied by slight modifications of sensibility. The diameters of the tactile areas become greater. Gradually new symptoms appear; at first a slight œdema along the inner surface of the tibia is met with, the face takes on a puffy, pasty appearance, by which the experienced physician at once recognises beri-beri, when as yet there are no other positive symptoms. At this stage also such subjective phenomena as palpitation, increased feeling of weight of the limbs and depression of spirits, usually appear. Objectively, one can in some cases already ascertain a slight enlargement of the right heart; at this early stage even the first sound of the heart is found prolonged and rough, and communicates the impression of cardiac "tumbling." Sometimes one already perceives the reduplication of the second sound, and an increase of sharpness over the pulmonary valve. The patient scarcely recognises what is

happening, and the affection develops with the precision almost of a geometrical progression, until a sufficiently acute increase in the symptoms shows the physician, as well as the non-professional man, that the condition of the patient is grave, and that his life is in danger.

The nature of the symptoms depends on the nerves attacked. Sometimes they are the nerves important to life, when a series of cardiac symptoms suddenly set in. The previously dilated heart may speedily give out, or acute dropsy of the pericardium cause syncope. On the other hand, it may be nerves connected with voluntary movement which are affected, or those of general sensibility, when the symptoms dependent on their lesions are met with; paralysis followed soon by muscular atrophy, as we have already described, accompanied by paræsthesia with severe pains, show that the disease has entered upon a new phase.

This exacerbation of symptoms may speedily end in death. Beri-beri of the rapidly destructive variety kills by paralysis of the heart. On the other hand, death may be caused by paralysis of the muscles of respiration, when altogether different clinical symptoms are present. It is rarely, however, that the patient succumbs so quickly, and in fact, in all these cases of apparently acute form, the disease is really chronic, and the acute accession may have for the first time attracted the patient's attention to the disease. But the well-marked degeneration of the dorsal muscles of the foot indicates that the disease has existed for a long time, and one can generally satisfy one's self of this by carefully analysing the clinical history, and paying attention to every detail of the recorded symptoms.

# CHAPTER V.

## SUBACUTE BERI-BERI—*Continued.*

### CONVULSIVE FORM—ATROPHIC BERI-BERI.

It would lead to confusion were we to endeavour to bring into one group all the cases which have been described under the name of subacute beri-beri.

The cases which we have described in the preceding chapter agree in one point, viz.—that the irritability of the dorsal muscles of the foot to the galvanic current was greatly diminished. By this symptom we could recognise the presence of the disease long before the patients knew they were the subjects of it; and so it frequently happened that the condition came as a surprise to the sufferer. The disease is, however, of a typically chronic form, and it is only in appearance that it presents itself under an acute form while entering upon a new phase. It is understood that this reasoning could not be applied to the native soldiers.

The first death from beri-beri amongst the native soldiers occurred six weeks after the arrival of the first battalion at Atjeh. It was therefore at first believed that the disease could not be estimated as lasting longer than six weeks at the most, but subsequent observation caused us to modify our views. It will be remembered that it was from amongst the men of this battalion that we selected those who were believed to be malingerers, and from the observations made upon them, we came to the conclusion that beri-beri was not a suddenly developing disease, but one running a subacute course. Therefore the belief that beri-beri is an acute disease, proving fatal in six weeks' time, is untenable.

There is one difficulty, in connection with the electrical condition of nerves, that we must endeavour to explain before pro-

ceeding further. Erb and Ziemssen have taught us that when a complete section of a nerve is made, one can ascertain, along with the qualitative modifications of the direct irritability of the nerves, an augmentation of this irritability for the continuous current. We have, however, recorded amongst the first symptoms a diminution of irritability. Therefore we might be accused of not having carefully observed the initial symptoms, or, at any rate, it might be objected that the modification in the state of the tissues, such as a slight œdema, &c., had so altered the distribution of the currents, that our definitions lost their value. This is why it has been peculiarly agreeable to us to point out that, in the true subacute form of beri-beri, some conditions, which, however different they may be from the preceding, are, to speak truly, a solid support to the conclusions which we have arrived at.

The symptoms observed in subacute and so called acute beri-beri, one would naturally consider, should present a different variety of nerve lesion to that met with in the purely chronic form; and it seems probable that the former, owing to the rapidity of its development, would more nearly resemble the condition met with as the result of the cut nerve.

In works on beri-beri, here and there mention is made of cramp in the limbs. Although it might almost be expected from the nature of the disease that cramps should occur, more especially during the exacerbations of the disease, we have only met with one case of real cramp in our experience, but this was a very well marked one. One may, it is true, in many beri-beri patients, come across some threatenings of cramps; but we have only once seen beri-beri of the convulsive type that Overbeck de Meyer has so carefully described. We record this case because of the great value we attach to it, as affording an excellent example of beri-beri of the subacute type.

CASE IV. (Subacute type).—R., a European, born in Friesland, aged 24 years, had resided for the last sixteen months in Sumatra. As a boy, in Holland, he had often had fever, but otherwise enjoyed good health. After staying a few days at Meester-Cornelis he left for Padang. In June 1886, he was sent to Atjeh, where he had very laborious duty at one of

the outposts. He remained there until November 1886, at which period he first felt ill, but continued, nevertheless, to carry on light duty of a less fatiguing nature. He continued to lose strength gradually for a month and a half, and then, with his legs swollen and painful, he entered the Panteh-Perak Hospital. Eight days afterwards he was sent to Padang.

*Clinical state on the* 10*th of February* 1887.—The patient is of robust frame, and had been physically strong and muscular. The mucous membranes are pale, his face slightly cyanosed, the tongue furred. He complains of pain in his legs, and an oppressed feeling in the chest, especially at night. The stools are regular; urine is without albumen; respiration costo-abdominal; he breathes at the rate of 40 per minute; pulse 116, small, weak, and irregular. No œdema except along the inner surface of the tibia. The heart's impulse is not noticeable when the patient is lying down; but when he sits up, the area of impulse becomes widely diffused, reaching as far as the fourth rib inside the mammillary line. There is also well marked epigastric pulsation. The area of the heart's dulness begins on the left at the third rib, and reaches as low as the fifth intercostal space in the mammillary line; on the right it can be made out only as far as the right sternal edge. The heart sounds are very feeble but pure.

(*a*) Physical signs in the *right* side of the chest:—Dulness on percussion commences in the mammary line at the level of the fifth rib, and is continued downwards over the liver. The dull area reaches a hand's breadth below the margin of the ribs, and behind it is limited by a line drawn from the lower angle of the scapula to the eighth rib. Within these limits vocal resonance is suppressed, and the breath sounds are feeble.

(*b*) Physical signs in the *left* side of the chest:—Posteriorly, the line of dulness is situated at a lower level. Above this line one hears a strong vesicular respiratory sound; below the line, as on the right side, the sound is scarcely audible.

(*c*) The organs of *motion*:—A great number of muscles appear enlarged, their bellies stand out prominently, they are hard to the touch, and painful when pressed; in the upper limb this is especially marked. The deltoid, the biceps, the long supinator, and the flexors and extensors of the fingers bulge enormously;

but in spite of their extraordinary size, which seems still greater on the left than on the right, the muscular force is much diminished. The dynamometer marks on the right 27°.5, on the left 14° only. The patient walks very badly, although the muscles of the thigh, especially the quadriceps extensor and the tensor of the fascia lata, stand out like cords under the skin. The patient moves the right leg more easily than the left. He cannot remain standing with the legs together, he can neither bend down nor get up again. Romberg's symptom is present. When the patient has his eyes closed he knows how the muscles of the upper and lower extremities are disposed, and can easily imitate the position that one gives them.

(*d*) The appreciation of pains is almost everywhere suppressed; the pricks of a needle are felt only on the inner aspects of the hands and shoulder joints, and over the hypogastrium as far as the umbilicus.

(*e*) The sense of touch has disappeared over the whole surface of the body except at a spot above the right groin; except at this spot, likewise, the patient can no longer distinguish the sensations of heat and cold.

(*f*) The reflex movements elicited by tickling the sole of the foot are present on both sides; cremasteric reflexes are present; abdominal reflexes are strongly marked; reflexes of the knee tendons are on the right feeble, on the left very strong; reflex movements of the triceps tendons are strong on both sides; no periosteal reflexes can be elicited.

While we are examining the sick man he is seized with cramp. The hand cannot voluntarily be supinated, flexed, or extended, and but feebly pronated; it is maintained in a position midway between flexion and extension, and owing to spasm of the muscles on the radial aspect of the forearm it is strongly abducted. The fingers are kept widely apart, especially the little finger. The fingers are bent upon the metacarpus in such a way that the respective phalanges are in a straight line. The thumb lies across the palm in a state of forced flexion, with the phalanges straight. The forearm is flexed upon the arm, whilst the latter is closely pressed against the body. The muscular spasm is stronger in the right arm than in the left. It is impossible to straighten the arm, or to replace

the thumb in its natural position. Everywhere a muscular bruit is heard, not only in the flexor and extensor muscles of the upper limb, but also in the muscles of the lower limb, which are likewise strongly contracted. The muscles of the face are not affected. The attack passes off in a few minutes, and is followed by the appearance of fibrillar contractions in the muscles of the extremities.

The nerves of the arm, especially the radial and median nerves, are mechanically very irritable; this is also the case with the muscles of the forearm, the flexor as well as the extensor group.

Electrical examination :—

INDUCED CURRENT.

| | Right. | Left. |
|---|---|---|
| N. External Popliteal, | 100+15 | 100+15 |
| N. Internal Popliteal, | 100+15 | 100+20 |
| M. Extensor Proprius Pollicis, M. Extensor Longus Digitorum, | As at 100+50 we were unable to obtain further contractions, we ceased on account of pain. | |
| M. Gastrocnemius, | | 100+42 |
| N. Median, | 35 | 30 |
| N. Radial, | 100+40 | 100+70 |
| | | Contraction very slow. |
| N. Ulnar, | | 55 |
| N. Facial, | | 50 |
| M. Flexor Sublimis Digitorum, | 60 | 84 |
| M. Extensor Carpi Radialis, | 100 | 100+40 |
| M. Levator Labii Superioris, | 50 | 50 |

CONTINUOUS CURRENT.

| | Left. |
|---|---|
| Nerve to Extensor Longus Digitorum, | 4 mA., Ka. Sc. |
| | 6 mA., Ka. Sc'., An. Oc. |
| | 12 mA., Ka. Sc'., An. Oc., An. Sc. |
| N. to inner head of Gastrocnemius, | 8 mA., Ka. Sc. |
| | 14 mA., Ka. Sc'., An. Oc., An. Sc. |
| M. Extensor Proprius Pollicis, | 10 mA., An. Sc. = Ka. Sc. |
| | Contraction extremely slow. |
| M. outer head of Gastrocnemius, | 5 mA., An. Sc. |
| | 8 mA., An. Sc'., Ka. Sc. |
| | Contraction extremely slow, long latent period. |
| N. Median, | $\frac{3}{4}$ mA., Ka. Sc. |
| | 4 mA., Ka. DT, An. Oc., An. Sc'. |

| | |
|---|---|
| *N. Radial, | 1½ mA. |
| | 2 mA., An. Sc'., Ka. Sc. |
| | 4 mA., An. DT., Ka. DT., An. Oc'. |

The primary An. Sc. has been observed three consecutive days in the nerve.

| | |
|---|---|
| N. Facial, | 3 mA., Ka. Sc. |
| | 8 mA., Ka. Sc., An. Sc'., An. Oc. |
| M. Flexor Sublimis Digitorum, | 1½ mA., An. Sc. |
| | 2½ mA., An. DT., Ka. DT., An. Oc., Ka. Oc. |

Contraction excessively slow, and the latent period very long.

| | |
|---|---|
| M. Extensor Carpi Radialis, | ½ mA., An. Sc., Ka. Oc., An. Oc. |
| | ¾ mA., An. Sc'., An. Oc., Ka. Oc. |
| | 1½ mA., Ka. Sc'.,Ka. Oc'., An. Sc'., An. Oc'. |
| | 3 mA., Ka. DC., Ka. Oc., An. DC., An. Oc. |

The contraction is very slow, and the latent period excessively long.

| | |
|---|---|
| M. Deltoid, | 5 mA., Ka. Sc. |
| | 6 mA., Ka. Sc'., An. Sc. |

The patient, whose temperature fell to normal, was sent a few days later to the hills.

The case we have just cited is especially important, because it proves, more than ever, how some apparent differences in symptoms can be grouped together under one heading.

We have here related the case of a patient who falls ill, after having passed several months in a country where beri-beri prevails. We hear from his own lips an intelligent account of its initial phase, and we find in several muscles of his calf a partial reaction of degeneration, sufficiently advanced to be diagnostic; and, as usual, it is the region of distribution of the external popliteal nerve which is first affected. On the other hand, in the nerves of the arm we meet with some remarkable phenomena; side by side, with a slight diminution of irritability to the direct and indirect Faradic current, we find a well marked increased irritability, to both direct and indirect galvanism, with some qualitative modifications. We might be inclined to ascribe it in some degree to the tetanic reaction that Erb has described. We believe, however, that these peculiar electric variations can be reconciled with the reactions of partial degeneration, for the qualitative modifications, the slow contraction, and the long duration of the latent period prove it.

From still another point of view this case is important; un-

fortunately we lost sight of the patient, and therefore we could not follow the development of his disease; but we would, with some reason, predict that he would suffer a rapid atrophy of the muscles, characterised by reactions of complete degeneration.

We think that in a similar case the indirect galvanic irritation will be found to decline rapidly, while direct irritation will remain a little longer, and will be augmented. Should it be so, we shall in that case have found that the course of the reaction is a little different in true subacute beri-beri. In the form just described, the initial phase progresses more rapidly, and when, at the end of six or eight weeks, the patient feels really ill, one finds in a large number of muscles a complete reaction of degeneration, with typical augmentation to direct galvanic irritation of the muscles.

It is quite possible that, in many persons suffering from beri-beri, a phase of irritation altogether distinct might present itself, accompanied by an increase to indirect galvanic irritability in several muscles. We have repeatedly observed in the nerves and muscles of the arm some reactions which resembled more or less those we have just described. Even assuming the above to be the case, the condition is quite compatible with everything stated, and as usual the importance of the nerves attacked controls the nature of the symptoms. When the nerve lesions are still further advanced, more extreme symptoms are met with, resembling more closely those which divided nerves show during the first weeks after they are severed. We give two more examples :—

Case V.—Minem, a native woman, having been a few weeks at Atjeh as a prostitute, entered the hospital suffering from syphilis. She was admitted on the 16th of January, and she first complained of feeling ill on the 8th of March. She developed paræsthesia along the lower extremities, pains in the knees, a slight œdema noticeable along the inner surface of the tibia, and she complained of palpitation. In a few days the œdema disappeared. Any possible variations of feeling which might have been present could not be observed, in consequence of her stupidity. The thoracic and abdominal organs were in a normal state. In fourteen days' time she was completely paralysed.

*April 2nd.*—All the muscles of the leg are atrophied; the movements of flexion of the leg upon the thigh, and the thigh upon the abdomen, are alone possible; when the leg is so bent, the patient cannot straighten it; all reflexes are suppressed. The muscles of the arms are also atrophied, especially the extensors, so that the hand hangs down as in a case of lead poisoning. The diaphragm scarcely moves in inspiration; respiration is costal, and 40 to the minute; the pulse is small and weak, 98 per minute. Except a slight increase of the area of the heart's dulness towards the right, there is nothing anomalous in the thoracic and abdominal organs. All the muscles of the leg are mechanically irritable; there is constant idio-muscular contraction, but no fibrillar twitching.

Electrical examination:—

INDUCED CURRENT.

| | Right. | Left. |
|---|---|---|
| N. External Popliteal, . . | not irritable | not irritable |
| M. Extensor Proprius Pollicis, . . | ,, | ,, |
| M. Tibialis Anticus, . . | ,, | ,, |
| N. Internal Popliteal, . . | ,, | ,, |
| M. Gastrocnemius, . . | ,, | ,, |
| N. Radial, . . . . | ,, | ,, |
| M. Extensor Communis Digitorum | ,, | ,, |
| N. Ulnar, . . . . | 60 | 50 |
| M. Extensor Carpi Ulnaris, . | 65 | 80 |

CONTINUOUS CURRENT.

| | Right. | Left. |
|---|---|---|
| N. External Popliteal (Right),. | 18 mA., not irritable . | |
| M. Extensor Proprius Pollicis,. | 2 mA. Ka. Sc. | |
| | 3 mA. Ka. Sc., An. Sc. | |
| M. Tibialis Anticus, . . | 1 mA. Ka. Sc. | |
| | 1¼ mA. Ka. Sc., An. Oc. | |
| | 2 mA., Ka. Sc'., An. Oc'., An. Sc. | |
| | 8 mA. Ka. DT., An. DT. An. OC'., Ka. OC. . | |
| All the contractions are extremely slow. | | |
| N. Ulnar, . . . . | 1¼ mA. Ka. Sc., An. Sc.' 8 mA. Ka. DT., An. DT. | 1¾ mA. Ka. Sc., An. Sc.' 8 mA. Ka. DT., An. DT., An. Oc'. |
| M. Extensor Carpi Ulnaris, . | 3 mA. Ka. Sc., 4 mA., An. Sc'. | 1½ mA. An. Sc. = Ka. Sc. |

CASE VI.—Ourip I, a sergeant belonging to Madoora, was admitted to hospital, after a seven weeks' residence at Atjeh, on the 21st of February, suffering from œdema of the feet and pains in the legs; there was, however, nothing anomalous in the walk.

*State on 3rd of March* 1887.—General weakness; anæmia of the mucous membranes; the pupils respond readily to light, and converge correctly; the tongue is foul, and dotted over with red spots; the pulse is small, a little tense, regular, 80 per minute, and after movement 108. The type of respiration is costo-abdominal, and regular. The œdema in the feet has disappeared; there is nothing remarkable in the gait; he can hop, stand on tip-toe, bend and recover himself with ease. Romberg's symptom is not present. The dynamometer in the hand indicates 90° for the right hand, 75° for the left hand. The last four dorsal vertebræ are painful under pressure. Nothing anomalous in the abdominal or thoracic organs.

*Sensibility.*—Feeling has diminished for light touches on the back of the foot and along the gastrocnemius; at the same places the patient cannot easily distinguish between hot and cold.

Diameter of the tactile zones in millimetres:—

| | Right. | Left. |
|---|---|---|
| Index finger, | 1 | 1 |
| Palm, | 8 | 7 |
| Back of hand, | 18 | 6 |
| Anterior aspect of forearm, | 25 | 53 |
| Posterior aspect of forearm, | 38 | 33 |
| Arm, | 34 | 50 |
| Chest, | 24 | 28 |
| Abdomen, | 26 | 24 |
| Hip, | 35 | 52 |
| External aspect of leg, | 42 | 49 |
| Internal aspect of leg, | 74 | 78 |
| Dorsum of foot, | 35 | 35 |
| Sole of foot, | 20 | 25 |

REFLEX MOVEMENTS.

| | Right. | Left. |
|---|---|---|
| Reflex by tickling soles, | present | present |
| Patellar reflexes, | ,, | ,, |
| Reflexes of the cremaster, | ,, | ,, |
| Abdominal reflexes, | ,, | ,, |

The muscles appear well developed. The gastrocnemius and anterior tibial muscles are seen even to bulge.

Electrical examination :—

INDUCED CURRENT.

| | Right. | Left. |
|---|---|---|
| N. External Popliteal, | 75 | 80 |
| On both sides contraction of all the muscles slow and persistent. | | |
| M. Tibialis Anticus, | 100 + 28 | 100 + 48 |
| N. Anterior Crural, | cannot be determined because of pain. | |

CONTINUOUS CURRENT.

| | Left. |
|---|---|
| N. External Popliteal, | 2½ mA. Ka. Sc. An. Oc. |
| Followed by slow contractions in all the muscles. | |
| M. Tibialis Anticus, | 11 mA. Ka. Sc. |
| | 6 mA. min An. Sc. |
| Contraction excessively slow. | |
| M. Extensor Proprius Pollicis, | ½ mA. An. Sc., Ka. Sc'. |
| Contraction very slow. | |
| M. Gastrocnemius, | 2 mA. Ka. Sc'., An. Sc. Ka. Oc. |
| Contraction excessively slow. | |

Some nerves, for example the anterior crural nerves, are very sensitive to pressure. In all the extensors of the hands we observe the reaction of degeneration.

In communicating these two cases our object has been to show, that whether beri-beri has lasted, as in the case of the Madoorans of the auxiliary militia, for a week or for a few months, the initial period presents characteristic features.

In our last case, that of a Madooran whom one would hardly have considered to be ill, we found, however, a partial reaction of degeneration; but it differed from the partial reaction of degeneration of the cases which had lasted longer in this, that the direct galvanic irritability had not diminished, or at least very little, while in some muscles it was even increased. This was, however, to be foreseen.

Let us now recapitulate once more, at the risk of appearing prolix, how according to us beri-beri commences:—(1) A vague feeling of heaviness, which at first increases very slowly, but which, having lasted for some time, leads the patient to seek advice; this is frequently accompanied by (2) a slight œdema along the inner surface of the tibia; or (3), the patient may become alarmed by palpitation of the heart; (4) when he presents himself for examination, it may be that a diminution

of the irritability of the nerves and of the muscles for the two currents already exists; (5) direct and indirect irritability in the area supplied by the internal and external popliteal nerves has ordinarily diminished; (6) there may be a partial reaction of degeneration, with a diminution of the direct irritability of the muscles of this group; in addition, one usually finds (7) some muscles bulging to an inordinate degree, and appearing to be really hypertrophied (perhaps an œdema already exists along the inner surface of the tibia); (8) a puffiness and pastiness of the face may aid in the diagnosis. The region of the gastrocnemius especially attracts attention, the muscle appears to be hypertrophied, feels hard to the touch, and is painful on pressure; (9) the skin over this muscle is almost from the first lessened in sensibility; (10) difficulties in walking are not necessarily visible; (11) the heart's area may be a little enlarged towards the right; (12) there is a reduplication of the second sound, and a loud pulmonary beat.

If the patient is allowed to reside in the place where he has fallen ill, the difficulties in walking may develop slowly. Complete suppression of irritation for the two currents may occur, with contraction which, although slow, is at this stage rarely absent, often without prevalence of An. Sc. over Ka. Sc. At the same time the right heart slowly dilates, resulting in a gradually increasing dropsy of the pericardium, and some other dropsical phenomena. The first symptoms of dropsy, the slight œdema along the inner surface of the tibia, may have, however, other causes. This progression in the course of the disease is not, however, always so slow.

Often when the disease has already made great progress, very sudden exacerbations take place, which manifest themselves by the following symptoms:—(1) In the sensory nerves: the patient complains of violent paræsthesia; all the nerves are excessively painful. (2) In the nerves of motion: stiffness, cramps, rapid paralysis in the muscles with secondary atrophy, and finally, a complete reaction of degeneration. (3) In the nerves of the sympathetic system: the most formidable effects are seen on the heart; in that organ a sudden dilatation of the right side occurs, which has been already becoming slowly dilated and hypertrophied.

The patient succumbs to angina, or to over-action of the heart; or perhaps the cardiac symptoms are less acutely aggravated, and instead we may have general œdema, alteration of the urine, and the usual train of symptoms consequent thereon. All these are followed by, if not immediate, at least almost certain death. To this series of phenomena belong perhaps also vomiting, which is considered to be of bad augury, diarrhœa, and a number of acute troubles often observed—gastric, laryngeal, and other crises.

Side by side with perfectly chronic cases, although the exacerbation might make one mistake them for acute or sub-acute cases of beri-beri, are those which really have a more rapid progress. Acute cases may prove fatal in five or six weeks; we have never seen death occur sooner, and we doubt whether beri-beri ever terminates more rapidly.

The initial phase, as seen in those patients who apply early to the doctor, differs from the preceding in these respects: (*a*) the partial reaction of degeneration is much better marked; (*b*) the qualitative alterations are more pronounced; and (*c*) the direct irritability of the muscles for the continuous current is never much diminished—ordinarily it is found to be much increased.

Noting the advance of the disease, one observes this initial phase of beri-beri transform itself, with or without an accession of fever, into beri-beri completely developed. Then the atrophies follow more rapidly; the danger of sudden death from heart failure is much greater—so great even that it might appear that it is for this reason that the development of a true dropsical form is rare, the patient being carried off before the dropsy has time to show itself. Armed with this knowledge of the matter we can now speak of "classic" beri-beri, and of its consequences.

# CHAPTER VI.

## ATROPHIC AND ŒDEMATOUS BERI-BERI.

EXTENT OF THE AFFECTIONS OF MOVEMENT—THE GAIT IN BERI-BERI—EXTENT OF DISTURBANCES OF THE SENSES—EXTENT OF THE VASOMOTOR DISORDERS—SYMPTOMS OF HEART DISEASE.

(*a.*) *Atrophic and œdematous beri-beri.*—As we have already seen, different authors are accustomed to distinguish an atrophic and an œdematous beri-beri. Between these two extremes, however, the most careful observers place a "mixed beri-beri." In order to render more intelligible what is meant by such a distinction, we give a photograph (see Plate I.), which we owe to the kindness of Van Eecke.

In the emaciated figure to the left every one will recognise the person suffering from atrophic beri-beri. He has beside him a person suffering from dropsical beri-beri.

Without wishing to deny that, clinically speaking, one might admit these two forms as of a different type, yet, it appears to us that by employing regularly the electric examination one could never have come to the conclusion to separate these two, and regard them as separate species of the disease.

Mixed beri-beri is the kind we most often met with at Atjeh, but in many cases the atrophy was so marked that we could with justice have spoken of an atrophic beri-beri; on the other hand, we saw cases in which the atrophy was so obscured by serous effusion into muscular and connective tissues, where the pericardium, pleuræ, and the peritoneum were so full of fluid, that we could with justice have called them dropsical beri-beri. Whatever may be the apparent differences between these cases, one symptom always remained constant, viz., the electrical modifications in the nerves and muscles.

We have already seen that in the initial phase death may happen without there having been any serious troubles as regards movement. We have found one group of cases which might have been considered as examples of acute beri-beri, but which are really exacerbations of subacute beri-beri proving fatal. We have observed the heart dilate in an hour's time, from the size of the hand until it reached beyond the border of the right side of the sternum; and in the autopsies we made in these cases we always found, besides the hypertrophy of the right side of the heart, dilatation of this organ, and generally slight dropsy of the pericardium, which was certainly secondary.

These cases naturally never form part of the extremes that we shall now consider.

For the production of atrophic beri-beri two conditions are wanting:—(1) The destruction of the nerves of motion is only partial, when the patient dies of heart disease. (2) Should this happen at the last moment, the nervous degeneration has been of too short duration to produce atrophy. The rapidly fatal course the disease ran is also the reason that dropsical phenomena have not time to develop.

Meanwhile it is clear that, when the disease has lasted longer, when it has made very great ravages in the nerves, a considerable atrophy of the muscles ought to result from it; but, on the other hand, degeneration may be very advanced in the nerves distributed to muscles without one finding any muscular atrophy; and yet again, in a certain number of cases an apparent muscular hypertrophy is not rare.

The polysarcous form of beri-beri described by Oudenhoven has been taken too little into consideration. In the mixed forms of beri-beri, the swelling of the muscles is never absent; it may result in part at least from an effusion of serum between the muscular fibres, but it depends certainly as well upon an enlargement accompanied by degeneration of the muscular fibres. These degenerated fibres which one finds at the autopsy are associated with fibres which are simply atrophied. It is probable that the swollen muscles atrophy more slowly, but we have not confirmed this point clinically. The reason of this is clear. Either the muscle becomes atrophied very rapidly when the nerve is completely destroyed, or else the patient dies from

cardiac troubles, or yet again he is sent elsewhere, or recóvers, so that he is lost to view.

On the other we have observed muscles become atrophied under our very eyes. (See Case V., given in broad outline.) The patients we have seen succumb to atrophic beri-beri had, as far as one can make out, all suffered from the subacute form of the malady. We give still another case in minute detail.

CASE VII.—B., a native sailor on board the Royal Naval steamer the *Gedeh*, aged between 25 and 30. The only history of previous illness obtainable was that as a child he had fever. Four years and a-half ago he joined as a soldier, but at the end of a year and a-half he caught beri-beri in the Moluccas, and was invalided out of the service in 1885. He recovered, so that he was able to again present himself for military service, was admitted, and sent to Atjeh, where he again fell ill. He was kept on board ship in the harbour for forty days, and was brought to Padang completely paralysed. He finally arrived at Batavia on the 24th of November.

*State on the 27th of November.* The patient is fairly well built: face a little puffy: pressure of the finger leaves no trace along the inner surface of the tibia, nor round about the ankles. The patient feels as if his arms and legs were being pricked with needles; he is especially sensible to pressure along his bones and muscles; he has no difficulty in making water or with his stools; he eats, drinks, and sleeps well. The pulse is small, feeble, and numbers 112 to the minute; respirations 32 to the minute. The right naso-labial fold is a little lower and less perceptible than the left; the angle of the mouth on the right side droops; the patient cannot inflate his cheeks when he has his lips closed, neither can he whistle. When he shows his teeth, the right angle of the mouth appears the lower, and the commissure of the lips on the left is more emphasized than on the right. He cannot draw the angle of his mouth towards the right. The type of respiration is exclusively costal, and the diaphragm descends but little, if at all, even with the deepest possible inspiration. The least pressure by the hand on the stomach is very disagreeable to him.

When the right hand hangs freely it maintains the following

position:—the hand is slightly flexed on the forearm; the proximal phalanges are bent over the metacarpus, the middle phalanges are flexed on the proximal, and the distal on the middle; the thumb is flexed and adducted. The patient cannot separate the fingers; he can easily flex them on the hand, but active extension of the fingers and the hand is altogether suppressed.

The dynamometer marks 2° in the hand. Flexion and extension of the elbow joint are possible, but have little force. Movements at the shoulder joint are possible, but excessively feeble. All the muscles are atrophied; those least affected are the deltoid, the biceps, and the pectorals. The left upper extremity is similarly affected with the right, but is still more feeble, the dynamometer marked 0. Muscular atrophy is strongly marked. The comparative measurements are as follows:—

| | Right. | Left. |
|---|---|---|
| Round the hand over the heads of the metacarpal bones, | 19.2 centim. | 18.8 centim. |
| Round the wrist, | 15.7 „ | 15.4 „ |
| Circumference of the thickest part of forearm, | 24 „ | 23.5 „ |
| Circumference round the belly of biceps, | 24.6 „ | 23.5 „ |

In the lower extremities the muscles are in a state of extreme atrophy. The limbs, as the patient lies in bed, are straight and slightly inverted. The soles of the feet are maintained in slight flexion, and he appears to be knock-kneed. All movements of the lower limbs are suppressed, with the exception of a slight power of flexion of both the knee and hip joints; the patient cannot straighten his legs when they have been bent.

Measurements round various parts of the lower limbs:—

| | Right. | Left. |
|---|---|---|
| Round the foot over the heads of the metatarsal bones, | 23.5 | 22.5 |
| Round the leg above the ankle, | 20.7 | 21 |
| Circumference of calf at the thickest part, | 32 | 31.6 |
| Round the thigh, | 42.5 | 42.2 |

He is unable to rise from a sitting position, he cannot turn on

his back; in a word, almost all the muscles are atrophied. The movements of the eyeball are normal; the tongue can be moved in all directions; the patient speaks and swallows without difficulty. All reflex movements are suppressed, except those of the pupil, which are made quickly and correctly. The pupils are equal.

*Sensibility.*—The slightest touch is immediately felt on the face and head; also in the mouth. On the chest and abdomen anæsthesia is complete. Above, the anæsthetic space is clearly limited by a line passing along the second rib; this line curves upwards, passes above the right shoulder, goes round it, descends behind to the upper part of the right arm-pit, and—crossing the axilla forwards—follows the anterior axillary line. This line serves as a limit between the anæsthetic area of the abdomen and chest, and the region of the back where sensibility is intact. On the left the line descends immediately, without going round the shoulder, along the anterior axillary line. Laterally upon the abdomen the anæsthetic limit is ten centimetres behind a perpendicular line drawn through the anterior axillary fold.

In the right arm the sense of touch has altogether disappeared, except on the back of the thumb, on the thenar eminence, and at the centre of the palm of the hand. In the left arm the perception of touch is confined to the centre of the palm of the hand. In the lower extremities the sense of touch has considerably diminished. The patient recognises a smart touch in only two zones of the right limb. The first assumes somewhat the shape of the sole of the foot, and extends along the external aspect of the calf, commencing ten centimetres above the external malleolus, and terminating at the back part of the knee. The second zone is limited below, fifteen centimetres beneath the groin, by a horizontal line which goes round the thigh; above, it reaches to the anæsthétic zone of the abdomen, and is bounded by a line drawn from the scrotum along the fold of the groin; it reascends to join the sensitive area of the back.

The sensation of touch on the groin is accompanied by severe pain, due probably to some pressure on the anterior crural nerve. In the anæsthetic area the patient no longer perceives the sensations of heat or cold. One may prick him without his

feeling pain, if one be careful not to press too deeply so as to affect the muscles. The strongest Faradic current is not felt.

The following muscles and nerves do not react under the influence of the induced current, even when it is very strong :—

N. Radial.
M. Extensor Secundi Internodii Pollicis.
M. Extensor Indicis.
M. Extensor Communis Digitorum.
M. Extensores Carpi Radiales.
M. Supinator Longus.
N. External Popliteal.
N. Internal Popliteal.
M. Tibialis Anticus.
M. Extensor Proprius Pollicis.
M. Extensor Longus Digitorum.

Diminished response to the induced current is met with on both sides in the following muscles :—

| | Right. | Left. |
|---|---|---|
| M. Flexor Sublimis Digitorum, . . | 100+80 | 100 |
| M. Palmaris Longus, . . . . | 100+80 | 100+50 |
| M. Biceps Cruralis, . . . . | 100+10 | 100+60 |
| M. Tensor Fasciæ Femoris, . . . | 100+10 | 100+60 |

In all contraction is very slow and persistent.

The sensibility of the anterior crural nerve to the continuous current cannot be determined, on account of the pain caused.

We shall give the results only for a few nerves and muscles :—

| | Right. | Left. |
|---|---|---|
| N. External Popliteal, . . . . | — | — |
| | Is not irritable. | |
| M. Tibialis Anticus, . . . . | 15 mA. Ka. Sc. =An. Sc. | 16 mA., Ka. Sc. 18 mA. An. Sc. Ka. Sc. |
| | Contraction is not very slow. | |
| N. Radial, . . . . . | — | — |
| | Is not irritable. | |
| M. Extensor Communis Digitorum, . | 2 mA. An. Sc. | 15 mA. An. Sc. 18 mA. An. DT., Ka. Sc. |
| | Contraction slow. | |

These suffice to show that in certain muscles there is a *complete* reaction of degeneration, while in a great number of other muscles one can ascertain a *partial* reaction of degeneration.

In the zygomatic branches of the facial nerve, and in the muscles around the corners of the mouth, one notices a partial reaction of degeneration. Here, as well as in a certain number of the muscles of the arm, direct galvanic irritability is augmented. The organs of respiration present no anomalies.

The area of dulness of the heart is increased towards both the right and left. The beat of the heart at the sixth intercostal space is strong. There is a reduplication of the second sound. The second pulmonary sound is sharp and loud.

The temperature rises regularly a little towards evening; for example:—

9th Dec., 36°.6 36°.6 38°.
10th „ 36°.6 37°.3 38°., &c.

The urine contains no albumen.

16th Dec., 1200 grms.; density 1015; turbid, neutral.
17th „ 1000 „ „ 1020 „ slighty alkaline.
18th „ 820 „ „ 1020 „ „ „

This patient succumbed to paralysis of the muscles of respiration, without having presented important physical signs.

Here we have a typical case of atrophic beri-beri; but whilst acknowledging the physical signs as few, it must not be forgotten that the heart was observed to be hypertrophied, that the face was pasty, and that the patient had considerable anomalies of the sense of touch.

In typical atrophic beri-beri we find all the cases resemble the above very closely, but the symptoms which characterise dropsical beri-beri are not altogether wanting; just as in the dropsical forms variations in the electrical reactions of the motor nerves are not wanting.

We have already often spoken of slight œdema along the inner surface of the tibia. This phenomenon, and the characteristic puffiness of the face, belong in fact to the earliest symptoms of dropsy that one notices in beri-beri. When one finds œdema associated with difficulty of motion, the variety is termed "mixed." A transient dropsy of the pericardium, or an œdema more or less marked above the ankle, can fairly justify their being ranked in this group. It is only when the œdema becomes general, when a pronounced dropsy shows itself in the

cavities of the serous membranes, that one speaks of dropsical beri-beri.

We give another case of mixed beri-beri, to show the great analogy that mixed beri-beri presents with the atrophic form in the objective, *i.e.*, the electrical, symptoms. The differences are :—

1*st.* By the side of some atrophied muscles one meets with hypertrophied muscles; although in atrophic beri-beri atrophy of the muscles predominates.

2*nd.* In the mixed form the electrical modifications are at times very diverse; they may consist only of a simple diminution of irritability of the nerves and muscles, affording a non-typical reaction of degeneration, although the typical partial reaction is not wanting. In atrophic beri-beri, on the contrary, typical partial reaction, or reaction of complete degeneration, is the rule.

3*rd.* Finally, that the symptoms of dropsy are more striking in that they are no longer confined to the face and the inner surface of the tibia, but are spread over the whole body. This is considered to be characteristic of dropsical beri-beri, but the same symptom not infrequently happens in the atrophic form.

Case VIII.—Saimoon, entered the army at Ambarava, in 1886, was placed in the depot at Meester-Cornelis, and on the 12th of August 1886 entered the hospital at Weltevreden. The state of the patient is described as follows :—

He is suffering from well-marked anæmia, but there is no enlargement of the spleen or liver; marked œdema in the thigh; increased activity of the heart, and greater frequency of the pulse; stiff gait, but no interference with co-ordination; muscular force good; reflexes in normal state; sensibility good; no albumen in urine. There is a well-marked abscess on the heel.

On the 21st of August, *i.e.*, nine days afterwards, he was reported fit for duty by the military commission; but on the 9th of September he was obliged to re-enter the hospital.

The history of the case on readmission was, that the patient had always been ill since he left the hospital; that the slight œdema of the thigh persisted, and that the patient became feverish and walked badly. From the 18th to the 20th September he

vomited repeatedly; on the 22nd of September he had an attack of fever, which yielded to quinine. January 17th 1887, the patient presents the following symptoms:—His puffy face clearly shows that he is suffering from beri-beri. There is marked anæmia of the mucous membranes; the pupils react well in every way; the muscles of the head, the eyes, the face, and the tongue execute all their movements readily; slight trembling in the movements round the left corner of the mouth; pulsation of the veins of the neck. The pulse, which is small and feeble, numbers 120 to the minute in repose; the type of respiration is abdominal and frequent. One distinctly feels the beating of the heart under the fifth rib to the inner side of the left mammillary line; the area of the heart's dulness commences at the second intercostal space, and reaches the right sternal border, on the left it reaches beyond the mammillary line to the extent of one inch. The sounds of the heart are pure but feeble; the first sound at the apex is prolonged; there is reduplication of the second sound at the base; the second pulmonary sound is louder than the second sound over the aorta. Slight enlargement of the liver and spleen can be detected, otherwise there is nothing anomalous in the organs of abdomen and thorax. Impressions made by the finger along the inner surface of the tibia and on the ankles remain. No atrophy of the muscles in the upper extremities; but in both right and left hands, spreading of the fingers, opposition of the thumb, and extension of the hand, are accompanied by trembling of the muscles concerned. In each lower extremity, to the outer side of the crest of the tibia, there is a furrow, which indicates an atrophy of the anterior tibial muscle. The muscles of the calf are hard, swollen, and painful on pressure. The patient walks badly, his gait is characterised by the difficulty with which he detaches, so to speak, his feet from the ground; on raising the leg high, and replacing the foot on the ground, he wavers. Romberg's phenomenon is ascertained to be present. He can neither raise himself on the toes, nor crouch down, nor get up again if he be placed in the latter position. The knees are flexed with but little vigour, and extended with a minimum degree of force. Dorsal flexion of the foot is suppressed entirely, and flexion of the sole of the foot very nearly so. The move-

ments of flexion and extension at the knee joint, as well as those of rotation, adduction, and abduction at the hip, are devoid of elasticity or strength. The patient cannot place himself in a sitting position in his bed, nor can he lie down again when placed in that position without collapsing. The reflexes of the sole exist as well as the reflexes of the knee; that of the right knee is augmented. The reflexes of the cremaster and of the abdominal muscles are present on both sides. The anterior crural nerve, the radial and external popliteal nerves, are very painful on pressure.

*Sensibility.*—The feeling of touch is suppressed over the whole of the lower limbs, except over a strip of skin on the external aspect of the calf of each leg. There is suppression also of the recognition of temperature. Farado-cutaneous sensibility is altogether suppressed in the lower extremities. A slight touch on the palm with the feather of a pen is not felt on either side.

The anæsthetic spots are not perfectly symmetrical on the two sides.

DIAMETER OF TACTILE ZONES:—

| | Right | Left |
|---|---|---|
| Index finger, . . . . . | 2 | 2 |
| Back of the hand, . . . . | 14 | 10 |
| Forearm (external aspect), . . | 15 | 40 |
| Arm, . . . . . | 15 | 60 |
| Chest, . . . . . | 20 | 30 |
| Thigh, . . . . . | 75 | 65 |
| Leg (external aspect), . . . | 50 | 65 |

The urine is without albumen, gives an acid reaction, and has a density of 1016; there is no sediment.

Electrical examination:—

INDUCED CURRENT.

| | Right. | Left. |
|---|---|---|
| N. External Popliteal, . . | 100+55 | 100+75 |
| N. Anterior Crural, . . . | 100+70 | 100+60 |
| N. Ulnar, . . . . . | 100+55 | 100+55 |

The contraction is very slow, and continues a long time. No contraction in the tibial muscle; in the left crural nerve only in the adductors.

| | Right. | Left. |
|---|---|---|
| N. Median, | 100 | 80 |
| N. Radial, | 100 + 90 | 100 + 100 |
| Contraction very slow and persistent in the extensor communis digitorum. | | |
| N. Facial, | 100 + 20 | 100 |
| Contraction slow. | | |
| M. Tibialis Anticus, | | not irritable. |
| M. Extensor Proprius Pollicis, | | ,, |
| M. Extensor Longus Digitorum, | | ,, |
| M. Gastrocnemius (inner head), | | ,, |
| M. Dorsal Interossei, | | ,, |
| M. Extensor Brevis Digitorum, | | ,, |
| M. Rectus, | | ,, |
| M. Vastus Internus, | | ,, |
| M. Rectus Abdominis, | | ,, |
| M. External Oblique, | | ,, |
| M. Adductor Magnus, | 100 + 70 | irritable. |
| M. Pectoralis Major, | 55 | 55 |
| M. Deltoid (median part), | 60 | 50 |
| M. Biceps (arm), | 90 | 100 + 25 |
| M. Triceps, | 100 | 80 |
| M. Palmaris Longus, | 100 | 100 + 50 |
| M. Flexor Sublimis Digitorum, | 40 | 90 |
| M. Flexor Carpi Radialis, | 100 + 50 | 100 + 50 |
| M. Flexor Carpi Ulnaris, | 100 + 50 | 100 + 70 |
| M. Supinator Longus, | 100 + 35 | 100 + 80 |
| M. Extensor Carpi Radialis, | 100 + 50 | 100 + 70 |
| M. Extensor Carpi Ulnaris, | 100 + 70 | 100 + 70 |
| M. Extensor Communis Digitorum, | 100 + 80 | 100 + 70 |
| M. Extensor Indicis, | 100 + 60 | 100 + 70 |
| M. Abductor Pollicis, | 100 + 50 | 100 + 78 |
| M. (third) Dorsal Interrosseous, | 100 + 50 | 100 + 70 |
| Contraction excessively slow, and persisting a long time. | | |
| M. Abductor Minimi Digiti, | 100 + 60 | 100 + 90 |
| M. Abductor Pollicis, | 100 + 80 | 100 + 65 |
| M. Sterno-cleido-mastoid, | 40 | 40 |
| M. Orbicularis Oris, | 80 | 75 |
| M. Levator Labii Superioris, | 100 + 35 | 100 + 45 |
| M. Biceps (thigh), | | not irritable. |
| M. Gluteal, | | ,, |
| M. Trapezius, | 60 | 50 |

## CONTINUOUS CURRENT.

| | Right. | Left. |
|---|---|---|
| N. External Popliteal, | 8 mA., Ka. Sc. | 6 mA., Ka. Sc. |
| | 15 mA., Ka. Sc., An. Oc., An. Sc. | 11 mA., Ka. Sc., An. Oc. |
| | | 14 mA., Ka. Sc., An. Oc., An. Sc. |

| | | |
|---|---|---|
| M. Extensor Longus Digitorum, | 20 mA., An. Sc. ♂ | 20 mA., An. Sc. ♂ |
| M. Gastrocnemius, . . | | not irritable. |
| N. to the Adductor Magnus, | 12 mA., Ka. Sc. | 12 mA., Ka. Sc. ♂ |
| | | 13 mA., Ka. Sc., An. Sc. ♂ |
| M. Adductor Magnus, . | 17 mA., Ka. Sc., = An. Sc. ♂ | 15 mA., Ka. Sc. = An. Sc. ♂ |
| N. Radial to the Extensor Indicis | 3 mA., Ka. Sc. | 8 mA., Ka. Sc. ♂ |
| | 6 mA., Ka. Sc'., An. Oc. | 9 mA., Ka. Sc., An. Sc. ♂ |
| | 9 mA., Ka. Sc., An. OC'., An. Sc. | |
| M. Extensor Indicis, . . | 14 mA., Ka. Sc., ♂ | 20 mA., Ka. Sc., An. Sc., ♂ |
| | 14 mA., Ka. Sc.', An. Sc., ♂ | |
| M. Extensor Communis Digitorum, . . . | 6 mA., An. Sc., ♂ | 11 mA., Ka. Sc., ♂ |
| | 8 mA., An. Sc'., Ka. Sc., ♂ | 13 mA., Ka. Sc. An. Sc.,♂ |
| N. Facial to the Orbicularis Oris | 7 mA., Ka. Sc. | 8 mA., Ka. Sc. |
| M. Orbicularis Oris, . . | 4 mA., An. Sc., Ka. Sc., ♂ | 6 mA., An. Sc. = Ka. Sc., ♂ |

At the end of three weeks we again submitted this patient to a long examination. We found a progressive aggravation in the whole of the muscular system, but that the dropsy of the pericardium and the diversities of sensation had remained stationary. He died a few months afterwards, while we were staying at Atjeh.

It is not astonishing that in parallel cases, where the heart has already suffered so much, there should be marked effusion into the cavities of the serous membranes. Nevertheless, we rarely came across these effusions in the epidemic that we witnessed at Atjeh, nor yet amongst the beri-beri patients we examined at Batavia. In the cases of two women, whom we could not examine with electricity, because of very severe dyspnœa which put their lives in danger, the effusion was very considerable. We communicate the following case of a man in whom the dropsical symptoms, although very considerable, were in great part of a temporary nature.

Case IX.—Djojodipo, aged from 25 to 30 years, has been two months and a half at Atjeh. He says he has been ill for fifteen days. The disease commenced by a tingling along the legs, and some pains in the calf and tibia. The legs after-

wards became œdematous, then he had dyspnœa, palpitation, and some difficulty in moving the lower extremities.

State on the 29th of March: The patient seems a strongly built man; the face is puffy, but the impression made by the finger leaves no trace; on the chest, however, the impression of the stethoscope remains. The lower extremities are swollen. The reaction of the pupils to light is normal, and the eyes converge properly. Conjunctivæ pale; lips morbidly blue; tongue swollen, dirty, and covered with red spots; a venous pulse is present in the neck. The pulse is small, weak, 92 per minute in repose, 126 after movement.

Type of respiration costo-abdominal; 36 per minute. There are no difficulties in swallowing or speaking; reflex movements are present on irritation of the cornea, the conjunctiva, and the throat; he executes all the voluntary movements of the lower extremities except those of the feet; he cannot sit up in bed without supporting himself on the hands; the patient walks with a halt, the right leg being more affected than the left. Romberg's symptom is absent.

All reflex movements are increased, the knee reflex is very strong on both sides; one cannot excite spinal epilepsy. The lower extremities are swollen, and the impression of the finger remains everywhere up to the knee; all the muscles of the leg are mechanically irritable, and present an idio-muscular contraction. The anterior crural and radial nerves are very painful to pressure; the external popliteal nerve is less so; the sense of touch has diminished all along the lower extremities; it appears to be the same with regard to the hands, but, we cannot make certain of this, as the patient is so stupid. We positively ascertain, however, that pricks with a pin are not felt along the lower extremities, when one is careful not to press on the muscles, which are very painful.

The beat of the heart is felt at the fourth intercostal space. The area of dulness of the heart commences at the third intercostal space, and passes two centimetres to the left of the mammillary line. One feels the beat of the heart three centimetres to the inner side of the line of the præcordial dulness. The dull area is greatest over the fourth rib, occupying at that spot an area of sixteen centimetres.

The boundary between the lung and the liver at the fifth intercostal space is not altered during respiration; dulness behind commences at the level of the seventh dorsal vertebra on both sides.

The sounds of the heart are pure but feeble; the respiratory sound, which disappears in the mammillary line at the fifth intercostal space when the patient is sitting up, reappears when he lies down; below, at the back, the vocal fremitus and resonance are absent; respiratory murmur is feeble everywhere. The liver can be made out to extend a little beyond the costal arch; the spleen cannot be felt; there is slight ascites ascertainable by palpation and percussion.

Electrical examination:—

INDUCED CURRENT.

| | Right. | Left. |
|---|---|---|
| N. External Popliteal, | 100 + 20 | 100 + 30 |
| M. Tibialis Anticus, | 100 + 40 | 100 + 25 |
| M. Extensor Proprius Pollicis, | 100 + 48 | 100 + 50 |

CONTINUOUS CURRENT.

| | Right. | Left. |
|---|---|---|
| N. External Popliteal, | 8 mA. Ka. Sc. | 8 mA. Ka. Sc. |
| | 12 mA. Ka Sc.', An. Oc. | 11 mA. Ka. Sc., An. Oc. |
| | 18 mA. Ka. Sc., An. Oc., An. Sc. | 18 mA. Ka. Sc'., An. Oc. An. Sc. |
| M. Tibialis Anticus, | 18 mA. Ka. Sc. = An. Sc. | 13 mA. Ka. Sc. |
| | | 18 mA. Ka. Sc'., An. Sc. |
| | Contraction slow, | |
| M. Extensor Proprius Pollicis, | 8 mA. Ka. Sc. | 10 mA. Ka Sc = An. Sc. |
| | | 19 mA. Ka. Sc'., An. Sc. |
| | Contraction slow. | |

There is no albumen in the urine. The morning temperature is 37.°8, evening 38.°7. It is diagnostic of beri-beri that there is marked dropsy of the pericardium, some dropsy of the pleuræ and slight ascites, accompanied by disorders of motion and sensation.

Eight days later the effusion had disappeared from the serous cavities; but the patient still walked badly.

We willingly admit that, in some other epidemics, the dropsical phenomena were more salient than was the case at Atjeh, but what we have seen of dropsical beri-beri has in no way shaken our opinion, that in this case also it is necessary to seek

the cardinal point of the diagnosis,—viz., the electrical phenomena and the disorders of sensibility.

(*b.*) *Extent of the Disorders of Motion in Beri-beri.*—The division of beri-beri into atrophic and dropsical does not appear to us to be necessary. We can very well dispense with it, because in the diagnosis of beri-beri œdema is only secondary, and if one takes the mixed form as the type, the dropsical form of beri-beri is nothing but a quantitative modification of it.

That which is more important is, for an instant, to direct our attention to the clinical phenomena presented by the motor system. We have already seen that in a beri-beri patient there may be present a swelling as well as an atrophy of the muscles; and, in the descriptions of the cases that we have given, one has clearly seen that the hypertrophied muscles and the atrophied muscles may equally be very painful on pressure. The swollen muscle is hard to the touch, as hard as a board; and during its contraction circumscribed swellings are often observed.

In the subacute cases one very often meets with an increase of the mechanical irritability; although, at the same time, a moderate blow inflicted on the muscle is followed by an idio-muscular contraction, a true sign of muscular exhaustion. This augmentation of the mechanical irritability frequently appears when the direct galvanic irritability has increased; especially when, during the test, one has to strive against tetanic contractions during the whole time that the current is passing. However, the increased mechanical irritability does not always keep pace with the augmentation of galvanic irritability.

We encountered a considerable augmentation of mechanical irritability of the motor nerves in the only patient attacked with convulsive beri-beri that we have examined. We noted similar symptoms in three other patients, but not to the same extent.

What is more important than these phenomena, is the peculiar distribution of the nerves affected, for it would appear to follow a definite course. In all our beri-beri patients we have found clinically, and let us say here, also anatomically, some disorders in the region of the distribution of the sciatic nerve. It would be superfluous to again enter into details with regard to this; we find, in short, complete reaction of degeneration, diminution of irritability for the two currents, and a partial re-

action of degeneration,—provided that one takes the last in its broad sense, as Stintzing has done.

The muscles supplied by the external popliteal nerve were always diseased, and almost always, and even more seriously, the flexors of the toes; then follow the extensors of the knee and the gluteal muscles. We have never seen any beri-beri patient, even amongst those more completely paralysed, who was not able to bend the knee. The flexors of the knee, the adductors, and the flexors of the thigh attached to the pelvis, remain healthy, relatively speaking, the longest. However, if the lower extremity has suffered so much that one already perceives electrical variations in the muscles of the thigh, the disease has generally made great progress, and we may be sure to find the extensors of the hand and fingers, and the long supinator of the forearm, also affected. The aspect of the hand is similar to that presented in lead poisoning. Succeeding the extensors of the hand, the triceps, the flexors of the hand and finally of the fingers, and the interossei muscles, are added to the list of those affected.

Once these muscles just mentioned are severely affected, there is no longer any question of regularity of sequence. The abdominal muscles, the diaphragm, and the intercostal muscles, may also suffer. In some cases we have met with paralysis of the diaphragm; in others paralysis of the intercostal muscles; in a third group both sets have been found affected simultaneously. We have often been able to ascertain that the paralysis of these vital muscles has been the direct cause of death. A large number of beri-beri patients succumb to paralysis of the respiratory muscles.

We have never found the sterno-cleido-mastoid or the trapezius paralysed, and we conclusively proved that the great pectoral and the biceps are amongst the muscles last affected. The cerebral nerves are not spared; of the eighty observations we have made, we have five times found the muscles supplied by the facial nerve attacked—four times the muscles around the angles of the mouth, and once the orbicularis palpebrarum. Even the muscles of the eyeball may not be spared, as we have observed one case in which the external rectus of the right eye was paralysed.

On the other hand, paralysis of the muscles supplied by the

hypoglossal nerve appears to be excessively rare. We have never observed it during life; and once only at the autopsy of a beri-beri patient did we find degeneration in the nerves of the tongue.

On the contrary, the muscles of the larynx are frequently affected. We believe, from what we observed in the case of two beri-beri patients who died suddenly, that paralysis of the larynx might have caused death. In the case of these two, we found the nerves of the larynx, the upper as well as the lower, greatly degenerated, but in spite of repeated examination, we could not ascertain, with the aid of the laryngoscope, any complete paralysis of the muscles of the larynx. With van Eecke, who was at the head of the immense hospital at Buitenzorg, where there were 1000 beri-beri patients, we examined forty of the hoarse patients. In time and place he will let us know the ultimate results of this examination, but we may safely say here that it cannot be a question of the paralysis of one muscle, nor of a physiological group of muscles, but rather a general paresis of all the muscles, a fact which was confirmed by what we found at autopsies.

One cannot diagnose that a patient has beri-beri by the suppression or the presence of reflex movements; when the disease is fully developed, all reflex movements in the lower extremities are suppressed. Westphal's symptom certainly then exists; but at the commencement, and especially in acute cases, there is no doubt that the muscular reflexes are not exaggerated. The cremasteric and abdominal reflexes are never suppressed, except in a very small number of cases.

(*c.*) *The Gait of Beri-beri Patients.*—As one might have expected, from such a wide-spread and irregular distribution of parts affected, there is nothing less typical than the walk of a beri-beri patient.

In the first place, the electrical variation may already be considerable, without the patient presenting any visible disturbances in his walking; but if he does present them, these disturbances are proportionate to the number and the functions of the paralysed muscles.

If the dorsal flexors of the feet, *i.e.*, the anterior group of leg muscles, are alone affected, the disturbance in walking is explained

easily enough by the absence of the action of these muscles. The foot can with difficulty as it were separate itself from the ground on which it rests. As it cannot be flexed on the leg, the extensors of the foot, *i.e.*, the posterior group of leg muscles, raise it very high, so as not to let the toes touch the ground when it is advanced, and the foot is seemingly thereby shot upwards. But if the extensors of the foot (*i.e.*, the posterior group of leg muscles) also suffer, and if the extensors of the knee and the muscles arising from the pelvis are affected, the disorders of motion are so complicated and present so much variety in different cases, that one cannot speak of any typical walk in beri-beri.

(*d.*) *Extent of the Sensory Disorders.*—In all our records of cases of beri-beri, disorders of sensibility are constantly found. We shall abstain here from speaking of paræsthesia, of the feeling of pain throughout the nervous system, or of muscular pains, as these symptoms are always present, and of them we have more than once made mention.

The sense of touch is always affected, and we are of opinion that the loss of the appreciation of space is a primary derangement. The diameters of the anæsthetic areas gradually become greater, and nearly correspond to the regions of skin over the bellies of the gastrocnemius muscles. The sense of touch is lost first on the internal aspect of the calf, then on the dorsum of the foot, and afterwards the anæsthesia is met with along the internal aspect of the leg. Finally, sensation may also disappear on the soles of the feet, and on the outer side of the leg. Along the groin, and immediately beneath it, sensation never disappears.

In the more serious cases, one finds at the same time some peculiar anæsthetic affections of the hands. Sensation is first lost on the anterior aspect of the wrist, and spreads over the skin, covering the hand in the following order :—the thenar and hypothenar eminences; the proximal phalanges of the thumb, of the little finger, of the fourth finger, and of the index finger, are successively affected; but the palm of the hand and the ends of the fingers are spared for a long time.

Anæsthesia affects also the internal aspect of the forearm, and extends along the inner side of the elbow joint, and may even

reach the shoulder. Finally, on the chest one sometimes observes a square anæsthetic spot which reaches as far as, or even below, the umbilicus. The region of the back preserves its sensibility intact.

In spite of repeated researches, we have not been able to find any anæsthetic spot round the mouth. As the distribution of anæsthetic areas just given agrees in the main with those described by van Eecke, Simmonds, and other observers in Japan, in all except the oral anæsthesia, we believe that it is simply by accident that we have been unable to discover it ourselves.

The diminution in the perception of cold and heat keeps pace with the diminution in the sense of touch, and is localised in the same manner.

Farado-cutaneous sensibility diminishes more quickly, and over a much larger area, a circumstance which renders it more easy to ascertain the electrical reactions by means of strong currents. The feeling of pain does not diminish so quickly; it may, however, diminish at a corresponding rate and in the same places, and even disappear altogether. When one wishes to establish the fact of the loss of the appreciation of pain in the skin, one must remember that the muscles and the nerves underneath the skin are painful on pressure.

The beri-beri patient is always conscious of the position of his muscles, and has no disorders of co-ordination, except those which proceed from the degeneration of groups of muscles.

(*e.*) *Extent of the Vasomotor Disorders.*—When one considers the peculiar œdema which commences on the inner aspect of the tibia, and in the face, it is natural that the influence of the vasomotor nerves should suggest itself. The variations presented by the sensory and motor nerves give one the right to do so.

This œdema follows to some extent the extension of the anæsthetic patch along the calf, but is most distinctly observable where the bone is immediately beneath the skin and presents a hard base to the pressure of the finger. At first the œdema is confined to this region. Beri-beri does not commence by œdema round the ankles; there is no reason therefore for making this leg-œdema dependent on the condition of the heart. This limi-

tation of the œdema partly explains the peculiar appearance which the swollen leg presents in beri-beri patients. One might compare it to a pear, of which the stem would be formed by the non-swollen ankle. The swelling of the belly of the calf muscles from hypertrophy meanwhile also contributes to give the leg this pear-shaped appearance.

This initial œdema is not only found along the inner aspect of the tibia, but is also met with on the face, where it gives the puffy, pasty look that is so characteristic; it is probable that the vasomotor nerves have to do with this also.

We again cite here a peculiar series of symptoms that one only sees occasionally. Van Eecke drew attention to the fact that in a certain number of cases, shortly before death, an acute swelling of the sub-maxillary and of the parotid glands appears. This must be considered a very grave symptom. The swelling does not proceed from an intra-glandular œdema, nor from a congestion of the blood vessels, but is associated with a swelling of the epithelium lining the acini and ducts of these glands. It is in all probability dependent upon nervous influence.

(*f.*) *Symptoms of Disease of the Heart.*—The heart is affected early in an attack of beri-beri, and hence arise a series of circulatory disorders, which constitute a very important train of symptoms. In addition to such subjective ailments as palpitations, spasms, and the like, an enlargement of the heart's area towards the right and a reduplication of the second sound, best heard at the apex, are frequently met with. The autopsy shows us marked hypertrophy of the right heart, accompanied by a dilatation still more considerable.

Later on it is notified that the nerves of the heart are pathologically affected, a conclusive proof that the heart symptoms should be attributed to the degeneration of the nerves. It is not possible to explain this hypertrophy satisfactorily, but it is easy to comprehend that the affected heart may at any moment cease to act. A clinical resemblance between over-action of the heart and angina pectoris is hereby brought home to one. It is also easy to understand that a chronically dilated heart, which empties itself so imperfectly, presents some difficulties to the flow of the blood from the veins—even the cardiac veins.

In consequence, it can be understood how dropsy of the peri-

cardium develops, at times rapidly, at times slowly, in harmony with the venous congestion; the appearance and disappearance of the pericardial effusion is also capable of being readily explained; nor is it at all astonishing that the heart, disturbed in its functions by dilatation and chronic hypertrophy, is no longer regular in its action, that general dropsy becomes manifest, or that sudden death should be the consequence.

Along with the cardiac affections, and more especially in acute exacerbations, symptoms associated with spasms and vomiting are frequently met with. Vomiting is considered, and not without reason, a very grave symptom; it much resembles in its character that met with in the gastric crises of locomotor ataxy. Relying on pathological observation, one attributes these vomitings to an affection of the terminal branches of the vagus. Considered from this point of view, the vomiting need not necessarily predict a fatal issue.

We have not come across any cases where we could diagnose an independent increase in the dimensions of the lungs; but, when a patient has died under our care, we have observed more than once, during an acute dilatation of the heart, that the limits of the lungs extended also. This dilatation was accompanied by rapid pulmonary œdema, a thing not to be wondered at under the circumstances.

# CHAPTER VII.

## CONCLUSION.

We are quite well aware that this is an incomplete description of the symptoms of beri-beri. We have made no mention of the higher senses; we have deliberately left unnoticed the rarer symptoms that present themselves; we have only spoken in passing of the paresis of the muscles of the larynx; we have not mentioned the trophic troubles in the skin, of the fall of the hair of the head or the beard, of modifications in the secretion of perspiration, or of many other notable conditions.

The field of our labour was so large that we were obliged to impose some limits. We believe, nevertheless, that we have added a couple of facts to those already known, and that the clinical evidence before us is sufficient to enable us to systematise the symptoms of beri-beri and recognise their import.

Merely from the clinical point of view, beri-beri is a multiple peripheral neuritis; it is a perfectly chronic disease, which can be early and readily recognised. Most prominent amongst the signs and symptoms, and not only of primary importance, but first in point of time, are the electrical modifications in the nerves and muscles of the leg which we have described. To these must be added disorders of sensation, accompained by various vaso-motor troubles; and very soon symptoms appear, at first only subjectively observed, which indicate that the nerves of the heart are also affected.

In most cases the disease progresses slowly; there is prolonged suffering where the functions of the motor and sensory nerves are gradually encroached upon; and when the vaso-motor system and the cardiac nerves are affected, œdema increases for a double reason. In such cases some accidental complication occurs and terminates the sufferings. Sometimes

a similar exacerbation may lead to death in a few days, sometimes even in a few hours; it may be because the degeneration of the cardiac nerves has advanced rapidly, or it may be that the degeneration has progressed slowly and surely. The heart fibres will carry on the work up to a certain limit, but when that is reached the sudden break down is easily accounted for by the increased strain thrown on the remaining fibres.

Sudden death, occasioned by a paralysis of the heart in beri-beri, and to which have been wrongly given the names, acute, *foudroyante*, etc., may occur at any stage of this disease. Along with this degeneration of the cardiac nerves, so terrible in its consequences, one meets with an exacerbation of the disease in other nerves, all of which has been described previously. The motor nerves may become affected after a few days' illness, symptoms of irritation and cramps ushering in the affection. We have shown the importance of this in our account of convulsive beri-beri. Cramps do not always appear; the more rapidly the motor nerves are destroyed, the more quickly complete paralysis and atrophy show themselves.

In atrophic beri-beri the patient usually succumbs to a paralysis of the organs of respiration, or a paralysis of the larynx.

If an exacerbation is not fatal it leaves the nerve impaired, and the patient approaches nearer and nearer to his end at each exacerbation. In fact, complete paralysis from complete destruction of the nerves is the exception.

When the motor nerves, the sensory nerves, and the vasomotor nerves are attacked at the same time, paralysis and cramps, anæsthesia and paræsthesia, œdema, vomiting, diarrhœa, etc., appear together.

It is by a consideration of these symptoms, apparently so different, but in reality depending on a common cause, that we have established the mixed forms of beri-beri. We have also drawn attention to the fact that, in mixed beri-beri, one encounters often, very often in fact, a swelling of the muscles, due really to their degeneration; and that this swelling probably precedes their atrophy. By this admission we accept Oudenhoven's term of polysarcous beri-beri.

If in spite of all these serious symptoms the patient does not succumb, in other words, if the heart does not completely give

out, one meets with the various phenomena associated with disturbed and uncompensated action of the heart; there may then occur, along with the œdema which we have been obliged to recognise as due to a direct nervous origin, some true œdema caused by venous congestion. Some symptoms of renal congestion, and of congestion throughout the whole body, characterise the forms of true dropsical beri-beri. However, there are symptoms which remain constant in beri-beri, whatever differences the details of symptoms present.

Baelz and Scheube struck the key-note of the disease when they found that a polyneuritis was the anatomical variation peculiar to beri-beri. We have confirmed their statements, and have been able to prove it in a systematic manner. Their strongest argument, however, was the anatomical demonstration of nervous degeneration in beri-beri; but this argument threatened to become weakened when nervous degeneration was shown to exist in a number of infectious diseases.

We have advanced a step beyond Baelz and Scheube's conclusions. We have given clinical proof that the electrical variations which the muscles and nerves present form part of the characteristic phenomena of the disease; and that from the commencement these variations are the surest guides to the knowledge of the existence of beri-beri. We believe that we have given to Baelz and Scheube's theory the support it needed.

# BOOK II.

# PATHOLOGICAL OBSERVATIONS.

# CHAPTER VIII.

## NAKED-EYE POST-MORTEM APPEARANCES.

After all that we have observed by the bedside of the sick, it is not astonishing to find that the dead bodies of beri-beri patients present very different appearances.

Every phase of the disease has upon it its stamp, so to speak. If muscular atrophy has predominated, one finds the bodies worn and emaciated, as one always does in the last stage of progressive muscular atrophy. These cases, however, are not numerous. Muscular atrophy and hypertrophy are generally found on the same body, accompanied by a slight swelling of the lower extremities. This circumstance, and the characteristic puffiness of the face, of which we have already spoken, enable experienced persons to recognise the body of a beri-beri patient readily. In addition, the manner in which the patient died is not without its influence upon the impression that the body makes upon us. As the cause of death is in almost all cases either a sudden stoppage of the action of the heart, or a paralysis of the respiratory muscles, the look of a person who is just dead is as horrible as his agony has been terrible: the blue and swollen face, the projecting eyeballs; the ecchymosed conjunctivæ, the jugular veins appearing under the skin like large blue bands, the mouth covered with froth, often made one at first suppose that the patient had died of suffocation. Otherwise the external aspect of the body presents no modifications of any importance.

Rigor mortis is not rapid; sometimes it does not supervene until two or three hours after death. On making an incision in the skin, the recognition of the two clinical varieties is easy and conclusive; in some cases the presence of serous fluid in the cellular tissue between and in the muscles of the abdomen points to the more dropsical form of beri-beri; in other cases, again, the

incision reveals the yellowish brown colour characteristic of atrophied muscles, and stamps the disease as atrophic beri-beri. In only two cases out of eighty-five autopsies did we find serous fluid. This is but an additional proof, if such were needed, of the slight boundary line between the two types of the disease, and when we remember that œdema has always existed at some period during the life of the beri-beri patient, the continuity of the two types is conclusive. We shall soon see that those cases where the quantity of serous fluid in and between the muscles and under the skin was considerable are in one point, and that too the most salient, in accord with those where the quantity was very slight, and in which for this reason atrophy was more apparent. This point is nervous degeneration.

Anasarca and the accumulation of serous fluid in and between the muscles are not the only symptoms which have a certain constancy in beri-beri. Almost all authors have mentioned dropsy of the pericardium as one of the characteristic features in the body of a beri-beri patient.

In our autopsies we have rarely found dropsy of the pericardium absent. In 64 autopsies we found

| | | |
|---|---|---|
| Little or no serous fluid | in | 2 cases |
| From 20 — 50 grammes | „ | 20 „ |
| „ 50 — 100 „ | „ | 13 „ |
| „ 100 — 250 „ | „ | 17 „ |
| More than 250 „ | „ | 12 „ |

Although one generally assumes that the death of a beri-beri patient resulted from dropsy of the pericardium, this opinion must be frequently wrong. The figures given conclusively prove that in most cases the quantity of fluid contained in the pericardium is much too little to have any signification as the immediate and mechanical cause of death; and we repeat, that even in those cases where one had ascertained during life that dropsy of the pericardium existed, the clinical symptoms very rarely showed evidence of compression of the heart. Besides, there is no doubt that the serous fluid in the pericardium, in a large number of cases, is the result of an effusion declaring itself a short time before death, or even during the death struggle.

However, the existence of dropsy of the pericardium is an important phenomenon, which, in a certain number of patients,

could be diagnosed during life; and it is in harmony with the pleural and peritoneal effusions which are met with in beri-beri. In the 64 autopsies cited above, we found hydrothorax 14 times, and ascites 9 times; consequently these œdemas are much less frequent than hydropericardial effusion. It is evident therefore that the presence of fluid in the large serous cavities of beri-beri patients is not the cause of death, but has only a secondary signification.

The large and small ecchymoses that we have met with in large numbers, in the visceral layer of the pericardium, and the visceral layers of the two pleuræ, are most certainly created during the death agony, and are in accordance with the way in which the patient dies. We found these ecchymoses no less than 54 times in these 64 autopsies.

The œdema of the lungs, which we have found less frequently (in 23 cases out of 64), is a phenomenon belonging to the last hours of a beri-beri patient; the same is to be said of emphysema of the margins of the lungs, which we have also noted on several occasions.

On the contrary, deviations from the normal are always met with in the heart, and are readily recognisable by the naked eye. In beri-beri hypertrophy of the right heart is always present; and, associated with the hypertrophy, there is always present a dilatation of the same side, sometimes small, at other times great, and not infrequently enormous. The left side of the heart may also be hypertrophied and dilated, but these changes are often in abeyance when the right side is pronouncedly enlarged.

We have never seen a heart which weighed less than 250 grammes (about $8\frac{7}{8}$ oz.). In 64 autopsies we found

5 of 250 to 300 grammes
42 of 300 to 350 „
10 of 350 to 400 „
7 of 400 to 450 „

The muscular coat of the heart is often pale, but to conclude therefrom that a fatty degeneration had taken place leads to error, as microscopic examination does not support the conclusion.

For the present we withhold the attempt to explain the hypertrophy of the heart and the accompanying dilatation. Hypertrophy of the right side of the heart is sufficient to ex-

plain the formation, more or less slow, or more or less rapid, of hydropericardial effusion, and the dropsy of other serous cavities. For it is evident when the right heart can no longer fulfil its functions, and empties itself incompletely, effusions in the serous cavities must follow, and in the pericardium most likely of all.

Accounted for in this way are the acute dilatation of the heart; the œdema of the lungs; the venous stagnation in the large veins of the neck, with or without deficiency of the valves; the true venous pulse; ecchymoses on the heart and in the pleuræ, even in the conjunctivæ; in a word, every symptom typical of the terrible death of a beri-beri patient. Beyond engorgement of the large veins of the right auricle and ventricle which one almost always finds at the autopsy, there is not much to say about the blood itself. To be sure it is of a dull red colour, it is saturated with carbonic acid, but we have not seen that tarry condition of the blood which is often spoken of.

As death is generally sudden, it is not surprising that no coagulated blood is met with in the ventricles, but it is incorrect to say the blood of beri-beri sufferers cannot coagulate. On the contrary, clots are met with, white or mixed, both in the right heart and the pulmonary arteries.

If we are asked whether a beri-beri patient might suffer from a progressive anæmia, we go back in the first place to what we have already said above. To this we add, that we have never found in beri-beri patients the well-known alterations in the marrow of the bones, although we have made special researches as to this point on ten bodies. On the other hand, besides the numerous ecchymoses of which we have already spoken, hæmorrhages into the muscles and between the muscles are found from time to time in different parts of the body. We have also observed them in the sheath of several nerves, amongst others the sciatic nerve.

In the large vessels of the arterial system we have never found any pathological changes other than slight symptoms of a commencement of endo-arteritis of the aorta, which are met with usually after a certain age in all bodies.

We have not remarked any important changes in the viscera peculiar to beri-beri. The spleen was often enlarged, and weighed more than the normal mean weight, but the experi-

ence of physicians in the East teaches us that in natives, as well as in Europeans who have spent many years in the East, much larger spleens are met with than those we have been accustomed to find in Holland.

As to the liver, there is nothing to relate except that it often appears swollen, owing to a venous hyperæmia, and that one sometimes even meets with the condition known as the "nutmeg liver." These modifications are all in accordance with the condition of the heart which we have described. As a curious fact, we may mention that in almost half of our autopsies we found an œdema of the walls of the gall bladder; even where there was no ascites.

There are no pathological changes to be recorded in connection with the kidney which are peculiar to beri-beri; not even where venous stagnation occurs is the kidney altered.

What we have just said as regards other viscera, is particularly applicable to the intestines. In the natives of the tropics especially, and also in Europeans who reside in the East, one finds more intestinal worms than in Holland, and one can understand why the *anchylostoma duodenale* is very frequent; but it would not be in accordance with known facts to conclude, from the presence of ten or twenty of the worms, that they are the cause of beri-beri, even when one finds isolated hæmorrhage around the cavity that the worm has made when it is fixed.

The *trichocephalus dispar* is, like the duodenal anchylostoma, a very frequent parasite; but neither is confined to beri-beri patients only, and they seem to be innocent enough.

In conclusion, therefore, we have to remark that, with the exception of hypertrophy and dilatation of the heart, which are the most frequent pathological conditions, occurring in 83 autopsies out of 85, no naked-eye changes peculiar to beri-beri were observed; and let us add at once that no modifications were found by the aid of the microscope either, so that we are still adrift as to the origin of the disease.

We have not yet recorded the results of our naked-eye examination of the nervous system. Let us frankly say at once that the fruits of such an examination of the peripheral nervous system are worth very little; it is impossible to recognise in this way the modifications it may have undergone. We found, on

four occasions, hæmorrhage more or less circumscribed in the sciatic nerve, and considerable local hyperæmia has not infrequently been recorded. We have very often been tempted to speak of a swelling or a discolouration, but microscopic examination has usually negatived the conclusion made from naked-eye observation, and taught us to be prudent, as fancy had here a large field in which to stretch its wings. In consequence we have not ventured to describe some peculiar signs which one meets in the nerves, although seemingly greatly degenerated. The organs of the central nervous system appeared as follows:—

Except for a very considerable hyperæmia, easily explained by the general venous congestion, we have not found in the brain or its membranes any modifications visible to the naked eye; neither the arachnoid nor the ventricular fluid was increased in quantity.

On exposing the spinal cord by dissection, nothing peculiar was generally observable on the dura mater; if a hydrorachis were present, it could not be considerable, as it was often difficult for us to gather, with a Pravaz syringe, a sufficient quantity of the spinal fluid for our bacteriological experiments. We did not find on the arachnoid or pia mater any thickened patches. All the natives of these regions have the pia mater covering the medulla oblongata, and the cervical portion of the cord, deeply stained with pigment. Often, it is true, some large tortuous veins, along the whole of the dorsal surface of the cord, struck the eye, but not more so than might be caused by the position of the body stretched on its back, and by the resulting venous subsidence. The cord is generally firm when it is examined in a sufficiently fresh state; we have never found any softening.

We ought here to observe, that the post-mortem phenomena in the East due to putrefaction have often been greatly exaggerated. Ten or twelve hours after death a useful autopsy can still be made, and excellent material can be obtained for microscopic researches.

Numerous authors have mentioned local softening in the spinal cord. Several of these descriptions rest simply on an ignorance of normal anatomy. When Huillet,[1] following the

[1] Huillet. Contribution à la geographie médicale de Pondichér. Archives de médecine navale, viii., December 1867, pages 420-425.

example of Beaujean, gives a description of a black softening, which occupies the cerebral peduncles from their exit from the pons Varolii up to the level of the crossing of the optic tracts, he is evidently speaking of the black substance of Soemmering, which is naturally found in beri-beri, as in other subjects. Several observers have described a form of softening which supervenes after death; these have not been confirmed by microscopic examination.

The spinal cord is very rich in blood, and hyperæmia of the anterior cornua is especially marked. We have found nothing worthy of note at either the anterior or posterior roots of the spinal nerves.

We very often imagined we saw some modifications in the roots of the nerves as they left the cauda equina; to the naked eye, what seemed a true discolouration, of a pale rose or grey colour, was demonstrated. However, after hardening the specimens in bichromate of ammonium, and staining the sections in osmic acid, we found we had mistaken perfectly healthy roots for diseased ones, and we came to the conclusion that no reliable results could be obtained from mere naked-eye observations. We believe, then, that a slight hyperæmia of the spinal cord is the sole modification perceptible to the eye; and that the pathological value is of small importance, as its presence is well nigh completely explainable as a result of post-mortem stasis.

With the exception of the heart, it is only in the voluntary muscles, and especially in those of the lower extremities, that the naked eye distinguishes any changes; one meets with atrophy and swelling of the muscles of the leg, and in the intermuscular cellular tissue often also a large quantity of serum. The colour of the muscles is observed to be altered; in the greatly atrophied muscles the dark yellow colour predominates, but in the hypertrophied muscles one meets with peculiar alternations of yellow lines and red patches of flesh, which give them a marbled appearance.

Having described what we observed with the naked eye, we will now give the results of a histological examination of the nervous system.

# CHAPTER IX.

## PERIPHERAL NERVES.

### (*a.*) NERVES OF THE LOWER EXTREMITIES.

We have already said that we award to Baelz and Scheube the credit of having been the first to demonstrate that the seat of disease lies within the peripheral nerves. Although we share their opinion, at least broadly, it nevertheless appears to us to be necessary to give a detailed description of the peripheral nerves affected.

On the one hand, we have observed some details that they have omitted to mention; and on the other, we have learnt to consider the disease of the nerves to be of the nature of a degeneration, and not of an inflammation. As previously stated, in 80 patients examined, the electrical variations of the muscles of the leg indicated an affection of the nerves; and as the result of the examination of 85 bodies, the nerves supplying these muscles were found without exception to be affected. Our method of investigation was as follows:—

The internal and external popliteal nerves, and their continuations down the leg, were carefully followed to their last ramifications, detached and raised. Each small branch was then spread, without tension, on a piece of wood, thereby straightening and fixing it, and finally hardened in a one per cent. solution of osmic acid, and washed in water. The period of exposure to the acid varied with the thickness of the nerve, but half-an-hour was the usual time required. After that the branch of the nerve was washed in distilled water, and the nerve, with its sheath, separated from the adherent connective tissue. To stain the nuclei the nerve was immersed in the alum-carmine solution of Grenacher, this method proving more satis-

factory than hæmatoxylin. After remaining in the solution an hour or more, the black filament was transferred to alcohol, and then to oil of cloves. In the clove oil the fibres were spread out, and with a little care it was quite possible to obtain a complete view of the fibres constituting a small branch. When extended in this arborescent fashion, it was quite possible to see and count the degenerated fibres in the branches of the nerve. In Plate II., figs. 3 to 11, the condition of the fibres met with is delineated.

In a nerve preparation obtained as described, it is usual to find a certain number of fibres in a normal or almost normal condition, and intermingled with these a certain number of degenerated fibres.

In the first place, one finds the well-known figures which the divided nerve presents soon after its excision. (Plate II., figs. 3, 4, 5.) The nerve fibre has become a little thicker, the medullary sheath is no longer a black cylinder with a double outline, but has broken up into masses.

Near Ranvier's nodes, the medullary substance appears to be altogether wanting; but midway between two nodal points it is collected into prominent masses. The axis cylinder is as yet unchanged. The conditions represented in these figures (Plate II., figs. 3, 4, 5) can never be confounded with any artificial products, and for the simple reason that with a little practice one can easily avoid all stretching of the nerve. Should one make artificial products, by not handling the fine fibres with sufficient delicacy, some assume the beaded appearance characteristic of the post-mortem changes met with in the medullary sheath, but they never present the rounded globules so characteristic of this phase of degeneration into masses. Besides, all those who have any experience of degeneration of nerves after being divided, and who have mastered the histological details connected therewith (a thing less simple than it appears), must know that there can be no confusion between a degeneration proper and artificial products.

The nucleated sheath of Schwann remains intact around this medullary substance as it lies agglomerated in masses. In some instances, one finds instead of the internodal nucleus two or three nuclei immersed in a mass of protoplasm somewhat swollen. The

axis cylinder of the nerve is to be found only in the vicinity of Ranvier's nodes, where the medullary substance has often disappeared over a large space.

If these figures are not always met with in the lower extremities, it is because clinical experience teaches us that the malady has been of too long duration. If an observer wishes good specimens, we would recommend that they should be looked for in the nerves of the larynx and the phrenic nerves. These nerves are not generally affected until a later stage of the disease, and their function is so important to life that it is not necessary that a large number be diseased in order to cause death. This phase of degeneration into masses we have often exclusively found there, as we have also not infrequently found it in the nerves of the extremities. By the side of these nervous fibres degenerated into masses, there is always found in the nerves of the extremities some other nervous fibres in a phase of more advanced degeneration. We have delineated some of them (Plate II., figs. 6 and 7).

It is no longer a question of nervous segments properly so called, as the medullary sheath has almost entirely disappeared. Here and there only vestiges of it are found in little masses, coloured black by osmic acid, and with Schwann's nucleated sheath stretched over them. Still more characteristic is it to find, at certain places, that the nerve fibres are filled with a number of little globules coloured black, brown, or dirty yellow, mixed intimately with a frothy mass, which becomes a clear rose colour when stained by carmine. Upon a superficial examination, these areas appear as fusiform thickenings of the nerve fibre. In this mass, or by its side, one always finds a nucleus; generally several are seen. Except at these enlargements filled with this frothy mass, the nervous fibre is everywhere very slender.

The nucleated sheath of Schwann, of which one always ascertains the presence round the fusiform swellings, has reduplicated upon itself, because of the absence of the medullary substance in the fibre. The contents of this fibre, for the most part very delicate, are stained by carmine a pale rose colour; they consist of a peculiár mass, upon which are seen numerous longitudinal lines, as though there were several very fine fibrils in Schwann's

sheath. These fibrils, often of a pale rose colour, lose themselves in the frothy mass which fills the fusiform thickenings. An uncoloured cone limits the frothy mass on each side, and it is there that the fibrillar structure of the contents, emptied of all else, is best shown.

The number of nuclei has greatly augmented; they are met with at regular intervals. There are all sorts of transitions between the phase of degeneration masses first described and the phase of frothy degeneration of which we have just spoken. Sometimes, especially in atrophic forms, the phase of frothy degeneration is the only condition observed (Plate II., figs. 6 and 7); but then some signs of regeneration are already found, of which we are about to speak.

It would be a great mistake to suppose that nothing more than the above mentioned changes are to be made out in a specimen stained by osmic acid; closer observation shows many other pathological points worthy of note. Almost at the first glance at the specimen, the attention is arrested by numerous fibres of extreme delicacy. The minute size of the fibres has, of course, but little to do with arriving at the conclusion that a nerve is degenerate; as, even after great experience, one may be misled were one to pronounce disease of a nerve to exist from that evidence alone.

But it is otherwise when one sees this thinning confined to some parts of a fibre, or when thin and thick segments alternate (Plate II., figs. 8, 9, 10), or when one finds so large an increase of nuclei, as is the case, for example, in Plate II., fig. 7. These attest, no doubt, the presence of an attempt at regeneration in the nerve. We ought to refer here to the figures that Gombault [1] has given, when he described his periaxile segmentary neuritis. The thin segments—"interposed segments"—have also been found by Renaut [2] in the nerves in their normal state amongst animals possessing solid hoofs. The fine segment is generally separated from the thicker by two of Ranvier's nodes. There is always found in the middle of the interposed segment an inter-

[1] Gombault. Archives de neurologie, 1880. Contribution à l'étude anatomique de la névrite parenchymateuse. Névrite segmentaire périaxile, p. 11 and p. 178. Compare figs. 13, 18, and 1, 2 and 7.

[2] Renaut. Archives de physiologie normale et pathologique. Recherches sur quelques points particuliers de l'histologie des nerfs, p. 161, 1881.

annular nucleus; at this point also the medullary sheath is very thin, but the nucleated sheath of Schwann is normal. It appears, moreover, that Schwann's sheath is very closely united to the endoneurium, at least one scarcely succeeds in seeing the interposed segment without adherent endoneurium. When these segments touch the larger fibres, the latter frequently show a row of globules with a double contour, coloured a deep black by osmic acid.

A little further on these give place to a continuous medullary sheath, which exhibits a double contour, coloured black, and often with a corroded aspect. In some very slender fibres it has happened that we have not observed any medullary sheath in the interposed segment (Plate II., fig. 8); but in the thicker fibres it is never wanting. The interposed segment is not only finer, but it is also shorter, than the normal segment. If several fine segments are met with side by side, the finest is always the shortest. Numerous transitions are met with: short segments with very fine medullary sheaths throughout, segments which up to the middle have a fine medullary sheath, and further on have a thicker layer. It is evident that in some conditions we have no attempts at regeneration present.

Whenever we met with this segmentary neuritis we found it almost exclusively in those parts of the nerves which were nearest to the spinal cord. In two external popliteal nerves, which we examined bit by bit, throughout their whole length, we found in the branches furthest from the centre the two phases of degeneration we first described; and in those which were nearer the centre we found a number of interposed segments amongst some fibres which were in a phase of lumpy and frothy degeneration. The nearer one approaches the centre, when the disease has not lasted a very long time, the more difficult it is to ascertain degeneration or regeneration by means of osmic acid; and we have not succeeded in finding any degenerated fibres in the anterior and posterior roots of the lumbar enlargement of the cord (compare also Plate III., figs. 1, 2, and 3).

Five peripheral nerves submitted to immediate examination in glycerine, with a solution of potash, showed an enormous increase of granular nerve-corpuscles; and on treating with methylene blue or with gentian violet transverse sections of the

nerves hardened in alcohol, numerous plastic cells were met with (Mastzellen). Additional results were obtained by carefully hardening longitudinal and transverse sections of nerves. We generally hardened peripheral nerves, as well as the central nervous system, by means of bichromate of ammonium.

We commenced with $1\frac{1}{2}$ to 2 per cent. solutions; then transferred the material into solutions of increasing strength, until after three or six days it was being kept in a 3 per cent. solution.

It is necessary to take care that the peripheral nerves are well spread out, without tension, and then hardened, if one wants to be certain of being able to cut them perpendicularly through their axis.

After the nerve has been placed in pure alcohol and dipped in oil of cloves, it is ready to be soaked with paraffin. The nerves so prepared are afterwards cut in sections, stained and examined.

The colouring was effected with Weigert's hæmatoxylin, by picro-carmine, with aniline blueblack and a number of other colouring matters for the nuclei, amongst which carmine impregnated with alum gave some very good results. However necessary the examination of sections of nerves may be, it cannot in any case give such good results as those obtained by dissection and teasing, in conjunction with osmic acid staining. Even in examining longitudinal sections of nerves, which have been hardened by means of osmic acid, one cannot judge with the same precision of the peculiarities that an isolated fibre presents as when it is prepared as above.

We shall now consider, in the first place, the results obtained by means of transverse sections stained by methods to exhibit the nerve nuclei.

They teach us, first, that one does not meet with an accumulation of nuclei around the blood vessels. The number of nuclei has increased, it is true, sometimes even to a considerable extent, but if we take into account what we have seen by the aid of dissection and teasing, we doubt whether these nuclei ought to be considered chiefly as products of the normal nerve nuclei or as blood products, especially since Hanken has shown that in nerve degeneration the nerve nuclei undergo segmentation.

The walls of the blood vessels may be thickened, and the connec-

tive tissue of the nerve is also frequently found to be thickened, and increased at the expense of the nervous elements.

One sometimes finds, especially alongside of a branch of one of the popliteal nerves, instead of a blood vessel, those peculiar bodies, with concentric structure, which Rosenheim[1] has described as existing in multiple neuritis. Like him, however, we believe that these are peculiarly obliterated vessels, and are simply the product of an acute attack. They are not met with in sub-acute beri-beri. (Plate V., fig. 1.)

We have rarely found any hæmorrhages, large or small, in the nerve.

Some very interesting objects are obtained when the nerves are treated by Weigert's hæmatoxylin method.

Sometimes (compare Plate IV., fig. 2, and Plate VI., fig. 1) one can show that almost all the nerve fibres have lost their sheath. Some rings, coloured black, have alone been left; these rings have a very beautiful effect on the yellow ground, and by enlarging the drawings of the preparations the condition is readily demonstrated. (Plate IV., fig. 2.) It is only in proportion as one approaches the centre of the nerve, of which the periphery was so greatly altered, or in proportion as one observes some nerves which have not suffered so much, that one perceives how much this method, otherwise so excellent, is inferior to that with osmic acid and the dissection of the nerve. It is difficult to give a precise signification to what one sees on the transverse section. This difficulty is not so great when the changes are far advanced.

If the black ring, which betrays the presence of the medullary substance, has altogether disappeared, if a granular lump fills Schwann's sheath, and has taken the place of the axis cylinder, and of the medullary sheath, these symptoms are very significant. Even when one finds a swollen axis cylinder, which in its transverse section touches immediately on a black ring of variable thickness, one finds oneself again in the domain of pathological modification and transition.

The test by means of longitudinal sections, in connection with the preparations obtained by dissection and teasing, always shows the degeneration described by Waller. The swelling into

[1] Th. Rosenheim. Zur Kenntniss der acuten infectiösen multiplen Neuritis. Arch. f. Psychiatrie, vol. xviii., fasc. 3, p. 782, 1887.

globules of the axis cylinder may be shown distinctly in the longitudinal sections.

At present, it is difficult to form an opinion as to the signification of the fine fibres, whether provided or not with the medullary sheath, that one meets with arranged in groups in the nerve. This makes one regret not having a good description of the distribution of the coarse and fine fibres in the principal nervous trunks in their normal state. And when one asks oneself, of a nerve trunk which is not greatly altered, or of a nerve for example which is near the centre, whether or not the number of fine fibres has augmented, one finds it is impossible, in the present state of our knowledge, to decide. It may be that the fibres are new formations, or mere atrophied products, or partly both, there is no means of knowing which. Sometimes one finds entire fields of fine fibres; when this is the case, there can be no doubt but that the fine fibres have augmented in number, and the nerve has undergone some pathological change. But it often happens that it is impossible to judge correctly, since one can only say that fine fibres are in the majority. Who then will be able to say that the number of these fibres bear a pathological or physiological signification ?

It is necessary to create for oneself, between the two extremes, a limit which is always a little arbitrary. It appeared to us, that in addition to the incontestable augmentation of these fine fibres in the nerves, which presented also an indubitable evidence of degeneration, the number of these fibres had augmented in the greater number of cases in the nerve trunks themselves.

The carmine stained preparations are indispensable, because the altered axis cylinder can be best seen in longitudinal sections; and the finer fibres show out better by their clear red colour than in the preparations made after Weigert's method. We have obtained therefore the same result as by the treatment of specimens with osmic acid. The nearer one approaches the periphery, the greater the nervous degeneration; the nearer one gets to the centre, the less distinct is it, and in the great nervous trunks, and in the roots, no changes are found; or possibly a slight increase in the number of fine fibres only.

## (*b.*) OTHER NERVES. NERVES OF THE HEART.

The degeneration that we have described, and which we have constantly found in the motor nerves of the lower extremities, exists also in the branches which lead to the skin of the leg. One generally finds it in the parts supplied by the saphena nerve. Nor is it confined to this region; in fact, the question rather is, "Do any nerves escape degeneration?" One point we can positively assert, and that is, that in all cerebro-spinal nerves examined we found in one case or other not only degeneration but advanced degeneration. The enumeration of all the degenerated nerves, and of the number of times we have come across them, can fulfil no useful end.

One point only deserves closer examination, owing to its great importance. If one carefully detach the nerve bundles, which, starting from the cardiac coronary plexuses, pass under the pericardium and into the muscular substance, and subject them to treatment by osmic acid and careful separation, one finds in the middle of the finer non-medullated fibres, other fibres, also more or less fine, with medullary sheath, which may present all the phases of degeneration. It is not rare to find there the phase of frothy degeneration; and more than once, on seeing this degeneration in nearly all the fibres provided with a medullary sheath, we failed to understand how the heart had been able to act so long. (Compare Plate II., fig. 11.) The small nerves of the heart are, however, so numerous, that the number of those examined, although actually great, was relatively small.

We will not pronounce any judgment with regard to the non-medullated nerve fibres met with here in such large numbers, because as yet there is very little known as to the degeneration of these nervous fibres.

We have systematically examined in five persons the different terminal branches of the vagus nerve. In the nerves of the larynx, which contain so many large fibres, this task was easy. In two cases we found an almost complete degeneration of the recurrent laryngeal nerve (compare again Plate II., fig. 4); twice also the superior laryngeal nerve was

found degenerated. One ought not to be surprised to find here merely the first phases of degeneration, if one thinks of the great physiological signification of these nerve branches to the economy.

The cardiac branches of the vagus nerve present still greater difficulties; especially is this experienced when examining the middle and inferior cardiac nerves, as before they reach the ganglia they contain almost exclusively fine fibres having a medullary sheath, or, what is equally embarrassing, some Remak's fibres, both coarse and fine. These nerves are separated with difficulty, on account of the large amount of connective tissue met with; and in fine nerves with a medullary sheath, confusions between the first phase of degeneration into masses and artificial products readily occur. Besides, one can well understand that very likely in these nerves degeneration has not had time to advance far, owing to the cessation of the heart's action consequent thereon; so that only exceptionally would one meet with an old phase of degeneration.

We possess a series of complete sections of all the lateral branches of two right vagus nerves, hardened in bichromate of ammonium, and stained partly by means of carmine and partly by Weigert's process.

However difficult it may be to form a judgment, we have nevertheless arrived at two conclusions, after repeated comparison with vagus nerves in the normal state.

In the first place, in the largest fibres of the right recurrent laryngeal nerve, beyond the place where it winds round the subclavian artery, as well as in the lateral inferior branches of the trunk, one can undoubtedly find some local thickenings of the axis cylinder, and a certain number of thick fibres filled with a granular detritus. Osmic acid had already shown on several occasions the presence of degeneration in the thick fibres.

Secondly, we find that the number of thicker fibres is less than in the normal vagus nerve, and that they have been replaced by a large number of fine fibres. (Compare Plate IX., fig. 4, and Plate X.)

For comparison, we have drawn as exactly as possible, a section of the trunk of a normal vagus nerve, by the side of that

of a vagus nerve of a beri-beri patient. (Plate IX., fig. 4, and Plate X.[1])

We now conclude this chapter, after having established the undoubted presence of a peripheral nervous degeneration in all the cases examined; and that this degeneration diminishes in intensity and in area in proportion as one approaches the centre.

[1] It is difficult for the reasons given to pronounce on the degeneration of the trunk of the vagus nerve. The degeneration in the nerve, of which we here give the figure, has been ascertained from sections of two laryngeal nerves by means of osmic acid staining; one will understand then that that would not have been more difficult in the thick fibres of the main trunk; further, it has been perfectly ascertained in the fibres of the heart, both coarse and fine, having a medullary sheath.

In the vagus nerve, beyond the place where the laryngeal nerve is given off, we have not observed any degeneration in the coarse fibres, and the augmentation of the fine fibres has been our only criterion.

# CHAPTER X.

## ANTERIOR ROOTS OF THE SPINAL NERVES; POSTERIOR ROOTS AND INVERTEBRAL GANGLIA.

We have previously stated that it is not possible, by osmic acid stainings, to ascertain any change in the medullary sheath of either the anterior or posterior roots of the spinal nerves, and further investigation by the examination of sections confirms what we said. Our researches extended chiefly to the examination of the roots of the 4th and 5th lumbar, and 1st and 2nd sacral nerves.

It was natural to examine these roots of the sciatic nerve, for a double reason, namely, that the branches of the nerve were always involved in degeneration, and especially as the normal anatomy of these roots had been carefully worked out by Luchtman. We also knew of Siemerling's work,[1] and by it we were made aware of the almost complete absence of fine fibres in the anterior roots of this region. We had also learned to know by his researches the distribution of the nebulous spots which Luchtman had already seen. With this knowledge before us, however, we never found modifications of any importance in the anterior roots. (Compare Plate III., figs. 1, 2, and 3.) We give a representation of the anterior root of the 1st sacral nerve in transverse and in longitudinal section, after staining with carmine. We obtained the specimens from the same subject as supplied us with materials for the drawings of the popliteal nerve (Plate IV., fig. 2, and Plate V., fig. 1; Plate V., fig. 2, and Plate VI., figs. 1 and 2).

From a study of these specimens it will be seen, that if there be any change at all, it is very minute; but however minute, it is a

[1] E. Siemerling. Anatomische Untersuchungen über die menschlichen Rückenmarkswurzeln. Berlin, 1887.

very distinct swelling of the axis cylinder in form of globules. From such an observation it would be rash to conclude that this slight swelling is the first sign of commencing degeneration.

It must not be forgotten that the axis cylinder is a very delicate tissue, that the autopsies are always made some hours after death, and that the hardening and other manipulations may easily alter the form of these delicate organs.

THE POSTERIOR ROOTS have given us much more trouble, and the best way of describing them will be to commence by an account of the ganglia associated therewith.

The anterior root passing from the spinal cord lies in contact with the anterior aspect of the ganglion, and joins the posterior root beyond the ganglion to form the nerve trunk. The posterior root springs from the ganglion of the root, and passes out to join the trunk; for convenience sake, however, we will term the posterior root all that tract from the nerve trunk up to the spinal cord. That part between the trunk and the ganglion is termed the peripheral portion, the part between the ganglion and the cord the central portion. We doubted many times as to the presence of a slight increase in the number of the fine fibres in the central part of the posterior root, but we found unexpectedly, in a case of transverse section of all the roots of the sacral plexus, a total loss of fibres at the 5th lumbar and the 1st sacral roots. This total destruction was accompanied by a secondary degeneration in the posterior column of the spinal cord; a degeneration that could be followed up the column of Goll. We give an illustration, because it appears to us to be important to know the place and extent of degeneration following the destruction of two lumbar nerves.

The roots were obtained from the case of a man who, some years before, had suffered from beri-beri, and who had succumbed to a so-called relapse. We did not examine the spinal ganglia; but this discovery induced us to carefully examine the spinal ganglia in subsequent cases.

We examined those of three patients, both by longitudinal and transverse sections; in one of these, the difference between the peripheral and central parts of the posterior root was very great. In the peripheral portion, there were some sections which

showed numerous fine fibres, which stained a bright red colour with carmine, and in which one could generally recognise fine axis cylinders (Plate IX., fig. 2). In the central part of the root the numbers of small fibres were less plentiful, and the proportion between the coarse and fine fibres was less than that of three to four, the number given by Siemerling (Plate IX., fig. 1).

In the ganglion of the root itself, we could not ascertain any peculiar variations, at least if we except some large pericellular empty spaces which existed between the endothelial lining of the nerve and the connective tissue investment.

In the two other cases, the differences between the central and peripheral parts of the root were not so marked; but here also, as regards the proportion between the coarse and the fine fibres in the central part, the coarse fibres predominated.

We have not therefore been able to ascertain any changes in the anterior roots, or at most only very slight ones. On the other hand, we have received the impression that long duration of the disease leads to an atrophy of the fibres in the part of the nerve situated between the nerve trunk and the ganglion of the root; the peripheral portion, in fact, of the posterior root. In the ganglion itself we found signs of change in cases of long duration, and not only so, but in the fibres proceeding therefrom in a central direction along the central portion of the root and the columns of Goll. Much the same change happens after the amputation of part of a limb, as proved by Friedländer, in the peripheral portion of the posterior root.

# CHAPTER XI.

## CENTRAL NERVOUS SYSTEM.

It is not without hesitation that we now pass to a description of what an examination of the spinal cord and of the basal ganglia has taught us.

We possess a series of preparations from ten spinal cords. Of two of these cords, we have made preparations of the part corresponding to the exit of each root, except in the dorsal region, where we have only done so for every third root. Of the other eight cords examined, we have only submitted the lumbar parts to a regular examination. In addition, we arranged a consecutive series of the whole of the 9th, 10th, and 11th cerebral nerves; and from three cases we have made numerous transverse sections of the medulla oblongata.

We have already mentioned in our macroscopic description that no changes are to be noticed in the membranes. Some transverse sections of the cord, with the membranes *in situ*, when examined by the microscope, confirm the absence of morbid changes.

Hyperæmia of the spinal cord, which is also visible to the naked eye, can be confirmed microscopically. The vessels always contain blood, more or less considerable in quantity, and best marked in the grey substance. Otherwise, there is not generally anything remarkable to be observed in the walls of the blood vessels.

Granular cells are not met with either after hardening, or upon an examination of the cord in glycerine and a solution of potash.

In all the cases we examined, the central canal of the cord was closed by a development of cells around its lumen. The cells had their origin in the epithelial lining normally existing there. In the periphery of the spinal cord, on the central

filament of the ependyma, along the posterior roots, on the two radicular tracts of the posterior column and on the lateral column, one meets with a variable number of amyloid corpuscles, but never a great number. The corpuscles are found also on the floor of the fourth ventricle, and along the roots of the vagus nerve.

Some transverse sections of the lumbar region, treated by Weigert's method with hæmatoxylin, are very instructive. In the great majority of cases the grey substance of the spinal cord is rich in fibres provided with a medullary sheath. The quantity of these fibres is never diminished so far as to fall below normal limits.

What we have said about the anterior cornua is applicable also to Clarke's columns, where the number of fine fibres with medullary sheaths is also very great. When, with the assistance of Weigert's method, one finds any change in the cord, it is found to be a diminution of fibres, in the neighbourhood of the exit of the posterior root from the periphery in the substantia gelatinosa.

To make this better understood, we give a drawing of a transverse section of the spinal cord at the level of the lumbar enlargement (Plate VII., fig. 3). We have also sometimes detected a similar attenuation of fibres where the posterior column touches the inner aspect of the posterior cornua. We have, however, always found intact the thick fibres of the posterior root which radiate in Clarke's columns.

Amongst these ten spinal cords we have found :—

| | |
|---|---|
| Perfectly normal, . . . . . | 6 |
| With some probable modifications, least marked in the two radicular zones, . . . . . | 3 |
| With some distinct alterations in the posterior column, . . . . . | 1 |

We have already said that we once found in two posterior roots a total absence of fibres with medullary sheath. Near the entry of these two roots the two radicular zones were altogether degenerated. In some sections, taken at a higher level in the lumbar region, one finds in the centre of the two posterior columns a degenerated patch in the form of a hammer. The tracts of degeneration, which appear to follow a fixed path, and

in which many of the fibres were destroyed, approach, as they ascend, nearer to the central region of the cord.

In the cervical enlargement, the right and left tracts have assumed a triangular form, and touch each other behind the central canal of the cord. Here one could still recognise, but in an irregular form, the presence of degenerated fibres, and could even trace them up the funiculus gracilis to the nuclei thereof (compare Plate VIII., fig. 2).

The study of preparations which had been coloured with carmine, after having been hardened by means of bichromate of ammonium, has not modified the opinion we had formed from examination of the specimens made according to Weigert's method. If any pathological changes were worthy of note, they existed in the posterior columns. A slight increase in the connective tissue of the cord was noted, and in some specimens a few axis cylinders had disappeared here and there, producing some true cavities, especially in the cords where we considered a slight degeneration of the radicular zones had taken place. The nerve cells of the anterior cornua sometimes presented slight modifications.

We found in all the spinal cords, and in every section, a great number of intact nerve cells, with well marked processes, large nuclei, vesicular in form, and with well coloured nucleoli, but we also always found some nerve cells which presented slight deviations from the normal.

In the first place, the pericellular spaces appeared to us much enlarged; naturally, no absolute value could be attached to this variation. We also found a certain number of nerve cells destitute of processes, no nuclei existed in some, and in others the nuclei occupied lateral positions, or actually lay against the linings of the cells.

A nucleolus was often wanting, and the whole cell assumed a less vesicular form than normal (compare Plate VIII., fig. 1, c, d, e). In a certain number of sections of the spinal cord we also found a few unfilled cells—possessing vacuoles in fact. The number of these was from one to four in a preparation which contained sixty visible cells. Finally, we sometimes saw in these cells a large quantity of pigment.

It may be that these modifications in the nerve cells are due

in part to the action of the fluids we used to harden the preparations; what might incline us to this belief is, that when the spinal cord was hardened in alcohol and stained, we saw in it some well marked processes, and a better colouring of the protoplasm of the cells.

It may be, however, that these departures from the normal are in reality of a pathological nature, although the modifications observed were certainly very slight. We did not meet with any swellings of the axis cylinder, or only to a very slight degree.

Some sections of the spinal cords, which had been treated with colouring matter, did not exhibit any augmentation in the number of nuclei. We are justified, therefore, in stating that the pathological changes in the spinal cord are insignificant. We willingly admit that we met with slight alterations in the nerve cells, and that the nervous tracts around the insertion of the posterior roots and the substantia gelatinosa were decidedly transformed, but none of these slight affections are proportionate to the pronounced degeneration described in the peripheral nervous system.

The examination of the medulla oblongata did not carry us a step further; in the only series of specimens we possess, and in the occasional sections we obtained from several other cases, we never observed any pathological changes. We have never met with any hæmorrhages. The only prominent condition observed was a layer of amyloid corpuscles on the floor of the 4th ventricle; and even in the nuclei of the vagus nerve, and the ascending roots of the 9th, 10th, and 11th cerebral nerves, were these corpuscles found.

In order to regularly demonstrate the pathological changes, it would now be necessary to submit the terminal organs of the motor and sensory nerves to a methodical examination. However, having regard to the time at our disposal, we were obliged to give up a detailed examination of the terminal plates and the peripheral organs of sense, and to occupy ourselves merely with the muscles.

There is no reason to believe that degeneration of the muscles does not advance evenly with the degeneration we have shown in the motor nerves. We have already drawn attention to the

yellow streaks, visible to the naked eye, that the muscles of most beri-beri cases exhibit.

By steeping a muscle which is not too atrophied in a physiological salt solution, and using a high microscopic power, one can always determine the changes brought about by beri-beri.

In those fibres which are not too impaired one still sees the transverse striæ, but they have a clouded appearance. The completely degenerated fibres reflect the direct light more strongly than the normal fibres; they appear of a brilliant white colour. The minute molecules, which are the cause of this strong reflection of light, disappear to a great extent when the specimen is treated with acetic acid, and at the same time a multitude of nuclei appear. When the muscle is treated with osmic acid, one sees that these molecules are, only very exceptionally, black in colour. In conjunction with these molecular changes, a less common condition is found, in which a fibre presents the appearance of a waxen thread with crenate edges. What mostly strikes the eye is the great difference in the thickness of the fibres. It is easier to judge of this difference when transverse sections are made; then, if a muscle which is not too atrophied be chosen, there will be found to be but a slight increase of the connective tissue of the muscle, no multiplication of nuclei, and but an insignificant modification in the walls of the blood vessels.

In the same field with the very fine fibres some very thick fibres are met with. In these fibres at times characteristic vacuoles are met with. We give here some measurements.

I.

Muscular fibres of a swollen fasciculus of a gastrocnemius muscle:—

| | |
|---|---|
| Average thickness of 50 fibres, . . | 155 $\mu$. |
| Thickness of the largest degenerated fibre, | 222.6 $\mu$. |
| Thickness of the finest fibre, . . | 94.4 $\mu$. |

Of these fibres, twenty-one exceeded the average, twenty-nine were below it.

II.

Muscular fibres of another swollen fasciculus of the same gastrocnemius muscle, in which more degenerated fibres were found :—

| | | |
|---|---|---|
| Average thickness of 50 fibres, | 132 | $\mu$. |
| Thickness of the largest degenerated fibre, | 222.6 | $\mu$. |
| Thickness of the finest atrophied fibre, | 47 | $\mu$. |

Of these fibres, twenty-six were above and twenty-four below the average.

III.

Muscular fibres of an atrophied gastrocnemius muscle :—

| | | |
|---|---|---|
| The average of 30 well recognised fibres, | 72 | $\mu$. |
| Thickness of the largest fibre. | 175. | $\mu$. |
| Thickness of the finest fibre, | 35 | $\mu$. |

Of these fibres, ten were above and twenty below the average.

In the average sized fibres, the transverse striæ can still be perceived, but in the thicker, which are generally rounded, instead of being of the more or less oblate hexagonal shape of other fibres, these transverse striæ have disappeared, and the muscular fibre is filled with a granular mass, in which very numerous nuclei are found.

If, however, one compares these preparations with those which have been obtained by teasing, or after having been hardened, it appears that this swelling is generally of a local nature, and that the fibre which shows some transverse striæ at the narrower parts, has lost them at the swollen parts. The augmentation of nuclei was also greatest at the swollen parts.

In addition to the variety of fibres recorded, namely, swollen fibres, fibres with a clouded look, and those looking like wax, some fibres are also found which are simply atrophied, and others in which the atrophy is accompanied by an increase in the number of nuclei, but which have kept their transverse striæ.

Be it understood that in the atrophied muscles, simple atrophy, with or without augmentation of nuclei, predominates. If, on the contrary, the muscle is swollen, the apparent hypertrophy is due in great part to the fibres swollen

in the beaded form, already described. (Plate VI., fig. 3, and Plate VII., figs. 1 and 2.)

The muscles of the heart show slight degeneration only. The fatty degeneration of the muscular fibres is excessively slight; the transverse striæ are preserved. Twice only have we found in the myocardium those little accumulations of cells, to which are attached so great an importance in death from diphtheria. However, as we have examined at least twenty-five hearts, in which no increase of cellular elements were discoverable, too great importance must not be attached to these incidental cases.

# CHAPTER XII.

## CONCLUSION.

ANATOMICAL examination is in perfect accord with the inference drawn from clinical observation, that beri-beri is a multiple neuritis. An extreme and very extensive affection of the peripheral nerves predominates; and as one approaches the central nervous system the pathological evidence of nerve change diminishes. The anterior roots of the spinal nerves are always healthy; but in the posterior roots one sometimes meets with a slight atrophy of the fibres, which is always infinitely less on the proximal side of the intervertebral ganglion than on the distal prolongation of the nerve. In the spinal cord, some variations of secondary importance are met with in the large nerve cells of the anterior cornua; but more constant still is a slight loss of fibres in the extension of the posterior roots in the two radicular zones, unaccompanied by any swelling of the axis cylinder granular degeneration of cells, or multiplication of nuclei.

We consider that we have established the claim that beri-beri be ranked amongst the diseases that are described under the name of multiple peripheral neuritis. However highly we esteem the work done by Baelz and Scheube, we consider that the proof has only now been given by us, inasmuch as we have clearly demonstrated that the nerves are attacked in the very first phase of the disease; and our anatomical observation has undoubtedly confirmed this affection of the nerves in a very great number of cases. In every beri-beri patient some symptoms of degeneration, as well as of regeneration, in the peripheral nervous system can be found.

We cannot be expected, in the record of our researches on beri-beri, to concern ourselves with the discussion that has been raised between MM. Erb, Strümpell, Eisenlohr, and others.

The question at issue, as to whether the alterations found in the anterior cornua are the cause, accompaniment, or result of the changes in the peripheral nerves, whilst the anterior roots are intact, is a matter of indifference to the end we have in view; and it is of no importance as regards the principal question. We have only to remark here that the progress of degeneration in the peripheral part of the cut nerve gives us no reason to suppose that, if a nerve cell be diseased, its extensions towards the peripheral nerve dies from the periphery towards the centre; therefore, as long as no absolute proofs are brought forward to support such a form of nerve degeneration, we cannot see why the multiple neuritis, established with so much trouble, ought to be classed amongst the diseases of the spinal cord as an anterior poliomyelitis.

# BOOK III.

# INVESTIGATIONS AS TO THE CAUSE OF BERI-BERI.

# CHAPTER XIII.

## PLAN OF RESEARCH.

EXPERIENCE teaches us that people inhabiting certain districts, buildings, or vessels, run a risk of being attacked by beri-beri. There must be therefore in these habitations a certain pernicious influence which one might infer would be the cause of the disease. This influence may be due to some inanimate material, a poison, which enters the lungs with the air, or the organs of digestion with the food or drink. On the other hand, it could also be due to a living organism which, developing itself outside the body, might enter and live as a parasite.

The investigation resolved itself into whether we were dealing with a chemical poison or a parasite as the cause of beri-beri. It did not seem necessary to consider other morbid influences. Beri-beri has often been attributed to insufficient nourishment, or to depression and melancholy; but we did not think these of sufficient importance to deserve consideration. The destruction on a large scale of the peripheral nervous system, such as one finds in beri-beri, must be attributed to a destruction of the nervous centres, or to a degenerative change immediately attacking the nerve fibres themselves. Such conditions can be brought about neither by hunger nor by sorrow. A certain weight may be attached to these as predisposing causes, but the true cause must be looked for in some influence from without, capable of destroying the nerve fibres. If this cause be due to a living organism, it certainly ought not to be found among the larger or more easily discoverable parasites. All that has been written on the larger parasites, and more particularly of intestinal worms, as the cause of beri-beri, has demonstrated pretty clearly that it is useless to search amongst these for a sufficient cause.

If beri-beri be due to a parasitic organism, it is certainly necessary to search for it among the microbes.

Granting this dilemma, poison or infection, the researches could be made in two different ways. Each of these two possibilities might serve as a point of departure. Once commenced in one of the two directions, the researches, whether they gave a positive or negative result, must help in elucidating the other side of the question.

The physicians who have of late studied beri-beri have generally come to the conclusion that, in all probability, the disease is of an infectious nature; and numerous observations on the propagation and the extension of the disease are cited in support of this opinion. We were uncertain, however, as to how far one could depend on what is narrated concerning the propagation and the presence of the disease, and this rendered it difficult for us to choose the direction we ought to take in our researches.

The choice was determined, however, by another consideration. If we wished to commence by seeking an answer to the question, whether beri-beri be due to a poison, we were immediately met by a great difficulty. Where and what sort of poison should be searched for? Experience threw no light whatever upon this; true it is, that some authors have supposed that fish and rice, the principal articles of food amongst the natives of the Netherlands East Indies, must be the vehicle of a poison causing beri-beri; but no serious support in favour of this opinion has been given; and even if we had wished to start with the supposition that beri-beri is caused by some poisonous substances, in rice for example, we had no means of knowing in what way we ought to conduct our researches, to arrive at a result of any value.

The difficulty concerning any deleterious gas in the air breathed was just as great as that concerning a poison introduced into the stomach with food. If we had decided to start from the hypothesis of poisoning, there was just as much reason to attribute it to a poison existing in the atmosphere, as to any deleterious substance contained in food or water.

Upon the other hand, our way was temporarily clearly indicated when we put to ourselves the following question:—

Is beri-beri a disease caused by living organisms? Were we

to start with that supposition, we would have to apply the methods which in recent years have given such wonderful results as to the knowledge of infectious diseases. The question might then be clearly formulated, "Can a living organism be found in the body of a beri-beri patient that is not to be found in a healthy man?" And if this be the case, "can this organism be cultivated outside the human body?" If the answer to this question were also in the affirmative it would be necessary to ascertain whether the simple cultivation of the microbe would give the same symptoms in animals as are observed in those suffering from beri-beri.

The rudiments of bacteriology afforded us the chance of giving a categorical answer to these questions. It was first necessary to make the researches arising from these questions, and should a profitless search have been made, then it would have been necessary to search in another direction, or to recognise that our knowledge is still too meagre to allow us to solve the problem.

# CHAPTER XIV.

## PRESENCE OF BACTERIA IN THE BLOOD.

We first asked ourselves the question, whether in the body of a sufferer from beri-beri any organisms could be met with which might be considered the cause of the disease? Our researches were at first made both on the dead and the living.

We commenced by examining sections of organs hardened in alcohol. Sections of the heart, kidney, spleen, liver, spinal cord, of several muscles, and of several nerves, derived from sixteen dead bodies, were systematically made. From each of these organs some specimens were coloured with fuchsine; others with alkaline methylene-blue in conformity with Löffler's method, a neutral solution of gentian-violet, and by Gram's method.

Never, in spite of observations made with the greatest care, by means of systems of homogeneous apochromatic immersions of $1\frac{3}{2}$ and $1\frac{4}{3}$ of Zeiss, did we succeed in seeing any micro-organisms, except in two cases, in which the autopsy was made about twenty hours after death. In these two cases we found large bacilli in the heart.

Afterwards, some cerebro-spinal liquid, taken from ten dead bodies, was put in some peptonised broth, with agar-agar. This was accomplished in the following manner:—After having washed the skin of the back with a solution of bichloride of mercury 1-1000, the vertebral column was exposed for part of its length with scalpels which had been previously disinfected by heat. The cut tissue was washed anew in the same solution; and then having removed the laminæ of two vertebræ very carefully, the dura mater was exposed to view for a short distance.

A little plate of metal, at a red heat, was applied to the dura mater, then, by means of a Pravaz syringe, we sucked up from the blister made, some drops of cerebro-spinal liquid, which

were immediately put into cultivation tubes. Before use the syringe had been rinsed more than once with a solution of corrosive sublimate, then with alcohol, and lastly with sterilised water.

In spite of all the precautions we took, the results obtained in this way were so uncertain that no definite conclusion could be come to. So we inoculated with the cerebro-spinal liquid nineteen tubes containing peptonised broth, thickened by agar-agar, and three tubes charged with gelatinised serum. Three of the agar-agar tubes, and one tube with serum, remained barren. In some tubes micrococci, in some bacilli developed, in others the two forms were united; a detailed description of which could be of no value.

From time to time we put some particles of the spinal cord, or of the peripheral nerves, in the nutrient jelly, but we did not obtain results to which any positive value could be attached.

Bacteriological examination of dead bodies presents, especially in the tropics, such great difficulties, that after experimenting for some time we found we were obliged to discontinue it, because for the moment it served no useful purpose. We were more inclined to do this as we thought it possible we might find bacteria in the circulating blood of those suffering from beri-beri. The method of procedure was as follows:—

One of the fingers of a beri-beri patient was well scrubbed and washed with soap and water, then washed with a solution of corrosive sublimate 1-1000, then dipped in strong alcohol, and finally sprayed with ether to make it dry rapidly. As soon as it was dry, a prick was made by means of a needle, previously disinfected by heat; and cover-glasses were charged with the blood and submitted to examination, either in the fresh state or after drying and staining.

The cover-glasses employed for these researches were first carefully purified in alcohol, and warmed at a flame immediately before being used. As a colouring medium, we generally employed methylene-blue, or fuchsine, which latter was prepared every day by adding a few drops of an alcoholic solution to boiled water, which was not only sterile but also deprived of dead bacteria which might have absorbed colouring matter.

This is the method we pursued in order to ascertain the pre-

sence of bacteria in the blood, or, at least the presence of minute bodies, which, as far as form and the absorption of colouring matter are concerned, had altogether the aspect of bacteria. At first the attempts at discovery gave only negative results; later on we found the reason.

At the commencement of our career at Batavia, with scarcely any exception, we only examined patients who had been brought away for some time from the place where they contracted the disease. The exceptions were two sailors, who had only fifteen days before left the vessel upon which they became ill. In their blood granular and rod-like bodies were found, which coloured with methylene blue. When we examined at Padang, and at Kajoutanam, the blood of those suffering from beri-beri lately arrived from Atjeh, we almost always found in them some bacteria, and at Atjeh itself none of the patients' blood was exempt.

Later on we recognised that at Batavia also bacteria could be found in the blood of those suffering from beri-beri, provided that the subjects were chosen from amongst those who were still living in the place where the disease originated, or who at any rate had only just left it.

As we have already said, we found both granules and rods, but amongst the latter neither the length nor thickness was uniform. Frequently the rods would only absorb colouring matter at the ends; sometimes also they had a form a little irregular, were unevenly coloured, or only slightly tinged. Generally the rods were more numerous, but sometimes the granules predominated. By the side of perfectly spherical granules some elongated granules were constantly met with, rendering it difficult to clearly distinguish between granules and rods. Granules and rods were often found united in little groups, and it was not unusual to see some granules resembling diplococci. In the fresh blood it is natural that the micrococci should be indistinguishable from granules of fat, or from other round corpuscles, which do not absorb aniline colours. Rods were often found divided into two by central constrictions. It was impossible to ascertain with certainty whether these rods were endowed with any movement of their own; but it must be admitted that it often seemed to us to be the case. It was impossible to come

to a decision on the point, because these rods could only be observed in the minute spaces of the preparations between the blood corpuscles, as when they were displaced at all forcibly, they escaped observation in the mass of corpuscles.

This displacement might always be due to some currents of liquid which, not being strong enough to draw after them a group of adherent blood corpuscles, were still strong enough to carry along a rod loosened in this way. The numbers of these corpuscles (that could not be mistaken for bacteria) found in the blood of those suffering from beri-beri, and even in different specimens from the same patient, were very dissimilar. In some cases they were in crowds in the whole preparation, while very often it was only after a prolonged examination that one succeeded in finding some rods or clearly defined diplococci. We give, in Plate II., figs. 1 and 2, a couple of preparations of blood, very rich in bacteria.

At Atjeh not only were they met with in those suffering from beri-beri, but when the blood of healthy persons who had passed sometime at Atjeh was examined the presence of bacteria was recognised.

We ought not to conclude therefore that these bacteria had no connection with the disease; quite the contrary, for at Batavia, in the blood of people who were quite well, and who were not placed in unfavourable conditions, we did not find any bacteria, either before our departure for Atjeh or after our return.

The blood of a healthy person who, for some years past, had inhabited countries where beri-beri did not exist, was examined the day after his arrival at Atjeh; it contained no bacteria: after a residence of a few weeks, however, both granules and rods were found in the blood. Again, we took observations of the blood of five people; four were apparently healthy, and one was ill with beri-beri. The blood of all five contained bacteria whilst at Atjeh, but they could not be found when these people returned to Batavia.

We could only conclude from this, that at Atjeh, where beri-beri is very general, pathogenic bacteria pass through the circulation of all, or of almost all of those living there. It is remarkable that at Atjeh the complaints of heaviness and of palpitation were general, even in people who passed as being in good health,

and some said they had noticed a swelling of a dropsical nature in their legs, without considering themselves as suffering from beri-beri.

For several reasons it was not desirable to go and search for symptoms of beri-beri amongst men who believed themselves to be in good health. On ourselves, however, and on our assistants, we were able to ascertain, besides the presence of bacteria, some symptoms which, however insignificant, were not altogether without pathological value—a feeling of heaviness, pains in the lower extremities, and palpitations. One of us developed a characteristic œdema of the leg, which declared itself at the end of the first fortnight of our stay at Atjeh, and did not disappear until he returned to Batavia. In all of us a diminution of the tactility of the skin of the leg was perceptible, which only disappeared at Batavia, and even then very slowly (see page 20).

We think, then, that some importance can be attached to the discovery we have made of the presence of bacteria in the blood of those suffering from beri-beri. That, in the tropics, bacteria are not found in the blood of healthy persons who are living under favourable circumstances, we have seen to be the case at Atjeh, in a person who was examined the day after his arrival; but more especially marked was this point at Batavia, where no bacteria were found even in the blood of those suffering from beri-beri, unless the patients had lately stayed in places where the disease was raging.

If at Atjeh, where the cause of the disease is undoubtedly very diffused, these bacteria were also found in the blood of persons who presented no striking symptoms of the disease, it is no reason why these bacteria should not be considered the cause of beri-beri, more especially now that it appears that even, in the case of people apparently healthy, some slight variations are present which accord with the symptoms of the disease.

# CHAPTER XV.

## CULTIVATION OF BACTERIA FOUND IN THE BLOOD.

THE microscopic examination of the blood could only lead to conjecture. No decision could be come to as to the pathogenic nature of the bacteria which exist in the blood of those suffering from beri-beri, until we obtained a pure cultivation of these organisms.

We tried to do this by taking a drop of blood from the finger, after having washed the finger as carefully as possible with soap, corrosive sublimate, alcohol, and ether, as we have before described. This drop, collected by means of a platinum wire, provided with a little ring at the end, and previously heated, was placed in a sterilised nutrient medium. We generally employed some peptonised broth, thickened with agar-agar; but we also used the serum of gelatined ox blood, cooked eggs, bananas, potatoes, peptonised broth without jelly, a decoction of earth with or without sugar, and finally, peptonised broth with gelatine, prepared in such a way that it remained solid, even in the high temperature of the tropics. This was obtained by boiling some broth, filtering it so as to separate the deposit of albumen, and then adding twenty per cent. of gelatine. After neutralisation and filtration the mixture was sterilised by heating it several times, and for short periods, up to 80° centigrade, and between the heatings rapidly cooling the mixture in ice. (Not infrequently imperfect sterilisation (with cleavage) is met with, more especially in the blood serum preparation, with the result that some of the tubes filled with gelatine present, at the end of several days, a development of bacteria; but this inconvenience is of no great importance, provided that the tubes are not employed until sufficient time has elapsed for them to have been properly tested as to whether they are barren or not.)

Although bacteria were always found in the blood employed for inoculation, the tubes for the most part remained sterile.

In fifteen cases, however, we obtained some growths of bacteria; from twelve patients growths of micrococci were developed in the tubes, and from three some growths of rod-like bodies. The rods differed from each other in every instance. Twice there were some bacilli, with a characteristic movement, although in one of the two cases they were much smaller than in the other. The third species of rod was very peculiar. In all the growths, in those which developed on a solid substance as well as in those which developed in a liquid, these rods, which were of very different lengths, and which were often not perfectly cylindrical but a little swollen in the middle or at one of the extremities, alternated with some spherical granules, which presented considerable differences in their diameters. Cultivated on some agar-agar, these bacteria formed a thick bed, with a shining surface,—at first of a white colour, which soon commenced to take a reddish tint, and which at the end of a few days was of a brick-red colour. The gelatine was not liquefied by these organisms. The same bacteria were once cultivated in some dust obtained from the air of barracks at Oleh-leh.

In the twelve other cases the tubes inoculated with blood showed micrococci. These developed best on the solid substances, where they formed a white bed with a shining surface. This phenomenon obtained in ten cases, but in two of the cultivations a yellow colour developed. Amongst the ten cases in which white growths were obtained, there was one composed of a single colony of micrococci, the members of which differed greatly from each other in size, and from which we did not succeed in obtaining further growths.

Sometimes from the same blood different bacteria were developed, but this did not happen when agar-agar and blood serum were used as the media. If in either of these a growth of bacteria took place, one could readily recognise by a plate cultivation that they consisted of one kind of bacterium only.

In the later days of our researches, the blood was mixed with nutrient gelatine, which was then poured on a cultivation plate, or dealt with in the way advised by Esmarch, namely, run on to the inside of a test tube held obliquely, and there

allowed to congeal. The last mode of manipulation has the advantage of preventing the bacteria of the air entering when pouring the gelatine into the tubes; a danger not great, it is true, when proper precautions are taken, but one which cannot be altogether avoided. The different colonies which developed on the bed of gelatine did not all resemble each other. We found on one occasion seven colonies of micrococci, of which two formed white, and five formed yellow growths. Four of these latter had a yellow-brown tint, and the micrococci generally had an elongated form, while the fifth had a yellow citron colour, and was formed of micrococci larger than the others, and arranged for the most part in bands of four. This last growth agreed with those which we had obtained in the above cases, where the blood gave in the one two colonies, in the other three colonies, all of micrococci, which had a yellow citron colour. Here also the tendency to the formation of bands of four was noticed.

In the course of our researches, we often asked ourselves if these different forms of micrococci ought to be considered as varieties of the same species. On several occasions, on making plate cultivations of one of the forms of micrococci, some colonies were obtained which did not resemble one another in the least, and which, placed on agar-agar, presented some differences in the form and colour which were there developed. But the consecutive generations cultivated on the same kind of jelly remained generally the same. It was only in the oblong micrococci that some difference in length of the same series was observed in the different growths on agar-agar, so that we could speak of a transformation of micrococci into rods.

We have also remarked on several occasions that when we placed in a fresh soil of agar-agar, a little of the old white growths of micrococci, kept for some months, some yellow growths of micrococci were developed, which sometimes grouped themselves in tetrad forms. But we cannot draw hasty conclusions from any of these observations. In spite of all the trouble we took, we could not succeed in discovering the circumstances which caused the transition from one form to another. If they had been found, and these transitions could have been produced at will, we would have been able, but only

then, to discard the supposition that it is the presence of other bacteria in the growths which gives rise to the phenomenon of transition.

Some further researches will be necessary to decide whether the different forms of micrococci that we obtained in our attempts at culture with the blood of sufferers from beri-beri, are of different species, or whether they are not some varieties of the same species. If we reflect that out of about eighty sufferers from beri-beri, in whose blood bacteria were found with the aid of a microscope, and were used for the purposes of growths, positive results were only obtained in fifteen cases; and when, still further, we consider that even in these cases the same kind of bacteria were not always obtained, a grave objection is necessarily raised against the value of the results that we have arrived at.

It may further be objected, that it is very possible that in any of these fifteen cases the bacteria did not occur in the blood, but arose from an accidental pollution during manipulation, and so entered the nutrient jelly. This possibility cannot be excluded with perfect certainty, unless one takes into consideration what we have just said. The danger of an accidental pollution in the growing of bacteria is great, especially in the tropics, where a laboratory will not easily be found in which the wind cannot penetrate by more than one opening, and where a puff of wind may not suddenly come to raise a crowd of living germs. Nevertheless, by extensive precautions, this danger can be obviated within sufficiently narrow limits. This has already been shown from the number of inoculations which we made, and which were followed by negative results. Besides, this objection loses something of its force when we see that in two of the fifteen cases where we obtained growths of bacteria, we found growths of micrococci which, although they were not all exactly the same, did not present, as we are about to show, anything but very insignificant differences.

These cultures were obtained partly at Atjeh and partly at Batavia. From the air of several rooms at Atjeh we could always readily cultivate similar micrococci, but never from the air taken in our laboratory at Batavia. So the supposition that these micrococci might not have proceeded from the blood

of patients, but might have come by accident in the jelly, is not very probable. It is otherwise in the three cases where each time some different bacilli were cultivated, because, under the circumstances, little value could be attached to them. For other reasons also, the examination of these bacilli did not allow us to admit any connection between these three kinds of bacilli and the disease.

# CHAPTER XVI.

## PATHOGENIC PECULIARITIES OF THE BACTERIA CULTIVATED FROM THE BLOOD.

FINALLY, to acquire some definite knowledge concerning the existence of a connection between these bacteria and the disease, it was necessary to find out whether these bacteria had the power of producing in animals any symptoms that might be put in the same category with those which are found in sufferers from beri-beri. The study of the disease has proved to us, in a convincing manner, that the symptoms of beri-beri depend on a degeneration of the peripheral nerves, and naturally the question arose as to whether the bacteria that we had found would produce in animals a similar degeneration of the nerves.

In researches on the pathogenic peculiarities of bacteria, it is a general rule that a single injection of a small quantity of micro-organisms ought to produce some visible symptoms of the disease, if the bacteria are really to be considered as the cause of the disease. The study of beri-beri has, however, taught us that this rule cannot be applied here. Beri-beri is an essentially chronic disease. The nerves are destroyed fibre after fibre; and when degeneration attacks any nerves which lead to the less important organs, it may have made great progress before the patient himself suspects that he is ill. It could not be admitted that these slow and progressive degenerations were caused by an organism which, when once it had penetrated into the body, developed itself there, slowly but surely, as is the case in tuberculosis.

What is opposed to it is, that not only were we unsuccessful in finding in the nerves the bacteria met with in the blood, but especially, and in a decisive manner, there is what experience has shown us concerning the genesis of the disease. This

experience taught us that it was not until after a residence of some weeks at least in a place where beri-beri was raging that an individual, in previously good health, could be attacked by the disease. It was not right, therefore, to seek the cause in a period of incubation of long duration, because then it would matter little whether the infected person remained in the infected place or not. If an individual susceptible of taking a disease such as measles, scarlatina, typhus, or small pox, has once been exposed to contagion, or if the virus of tuberculosis or of syphilis has penetrated into the body, it matters little, as regards the symptoms of the disease declaring themselves, whether he renews contact with the source of the disease or keeps distant from it.

It is otherwise with beri-beri. Those only are attacked who have lived continuously for a considerable time in the places where the disease is rife. To go into a place where the disease is not raging is not only the best means of cure, but is also a means of preventing the disease developing further, even after the first symptoms begin to show themselves. That is the reason why, when some animals have been inoculated with blood from beri-beri patients, the results have always been negative; it was not therefore allowable to conclude from such results that organisms causing beri-beri were not present in the blood.

We also made a couple of experiments of this kind. We injected into the abdominal cavity of a monkey 25 cubic centimetres of defibrinated blood, taken a few minutes before from a beri-beri patient in a state of dyspnœa, and in whose blood a considerable number of bacteria could be detected by the microscope. In the case of another monkey, we introduced under the skin of the thigh a piece of the popliteal nerve taken from a beri-beri patient who had died a few hours before. In neither of these animals were any symptoms of beri-beri noticed, but the second monkey, 22 days after the nerve had been put under the skin, developed symptoms of tetanus, to which the animal succumbed at the end of a day and a half. The tetanus was probably caused by a wound which the monkey had made by the rubbing of his collar. We were assured that captive monkeys often succumbed to tetanus in consequence of

slight wounds. The wound made by the introduction of the nerve was perfectly healed, and the embedded nerve itself, enveloped by a tissue of new formation, was recovered with difficulty. No degeneration in the nerves was met with. As only repeated experiments could cause the disease, we did not further pursue this kind of test. To often make inoculations with parts of dead bodies in the same animal seemed an unsatisfactory method of experimenting, and the repeated injection of blood taken from the living was contrary to the interests of the patients. From time to time it may happen in the case of a sufferer from beri-beri, who has sensations of suffocation, that bleeding is not only harmless but may be useful; however, as a general rule, the blood of a beri-beri sufferer is generally of too much value to the patient to allow it to be taken for the purpose of experiments. The injection of cultivated bacteria under the skin or in the abdominal cavity can, however, be made and repeated without great inconvenience.

We provided ourselves at first, for purposes of injection, with micrococci from the white growth variety. These were obtained nine times, as we have said above, except in the case, also mentioned, where a single white colony developed, composed of micrococci ranging greatly in size, of which it was impossible to continue the cultivation. Of these nine growths, there was still another which could not be examined, because the tube of agar-agar, inoculated with some blood in which micrococci were developed, was lost.

The eight remaining growths did not, however, completely resemble each other. Whilst six possessed the faculty of liquefying gelatine, the two others did not.

We think that this difference ought not to be considered as of a specific nature, as we shall attempt to show further on. Provisionally, however, we shall only speak of the micrococci proceeding from the six growths where the gelatine was liquefied. Inoculations with this micrococcus were made on rabbits and dogs. The bacteria were cultivated in simple broth or on peptonised broth with agar-agar; in the latter case, they were held in suspension in a neutral solution of sea salt for injection; this was done subcutaneously, or in the cavity of the abdomen, with a small Pravaz syringe previously disinfected with a solu-

tion of corrosive sublimate, then washed in alcohol, and finally with sterilized water.

We here give the results that we obtained in this way:—

1. Rabbit. Four injections under the skin in nine days. The eighth day the animal is unable to stand; the next morning the animal is found paralysed in both its hind legs; it died soon after with violent dyspnœa. Upon opening the thorax half-an-hour after the respiratory movements had ceased, the heart was still contracted. An abscess was found under the skin at the spot where the injections had been made. Recent and extensive degeneration was evident in the different nerves which lead to the muscles of the hind legs; no degeneration was found in the phrenic nerves.

2. Rabbit. 23 subcutaneous injections were made in 25 days, and then the animal was slaughtered. At the autopsy, several abscesses were found under the skin, some ascites, and, on the left side of the chest, a purulent pleurisy. No degeneration of the nerves was found.

3. Rabbit. 21 subcutaneous injections, including 5 in the abdominal cavity, in 44 days; at the end of the period, the animal, although lean and slow in its movements, did not, however, present any evident symptoms of disease. Four small abscesses under the skin were found, and between the bladder and the rectum a small quantity of a fibrinous exudation. In several branches of nerves in the hind legs signs of degeneration were pronounced, some recent, but most of old date. The phrenic nerves exhibited similar signs.

4. Rabbit. 20 subcutaneous injections in 42 days. The animal was killed while showing only a little slowness in movement, but otherwise apparently healthy. In the left hind leg, as well in the upper as in the lower part, a considerable degeneration of several branches of the nerves was found, but not so in the right leg.

5. Rabbit. 14 subcutaneous injections in 48 days. The animal when killed showed no abscesses subcutaneously. Nerve degeneration in the hind legs was well marked.

6 and 7. In the case of two rabbits, one male and one female, which had been placed in the same hutch, we tried to produce infection by simply placing each day a growth of bacteria in the

hutch. After having passed 56 days in the hutch so infected, the two rabbits were killed. In the male as well as in the female, which had littered in the interval, the nerves in the hind legs were found in a state of degeneration.

8. Dog. 17 subcutaneous injections in 36 days. In the course of the experiment, as a consequence of the injections, there appeared 5 abscesses, each of which was opened as soon as it appeared. During the last few days of life, the dog did not jump as well as usual. The animal was killed on the 36th day, when, in several branches of the nerves in the hind legs, nerve degeneration was found.

9. Dog. 14 subcutaneous injections in 23 days. When the animal was killed no nerve degeneration was found.

We again made three experiments with the same micrococci, which were not taken from a culture of human blood, but from the blood of a rabbit, which had a degeneration of several nerves, after having been infected by a mixture of bacteria drawn from the air. (See further on at page 133.) The results obtained were:—

10. Rabbit. 5 injections in the abdominal cavity in 21 days. When the animal was killed, some filaments of fibrine were found between the intestines; and nerve degeneration, more especially of the branches of the nerves which supplied the muscles of the hind legs.

11. Dog. 5 subcutaneous injections in 16 days. Within 3 days after the first injection, the dog commenced to show symptoms of paralysis of the hind extremities With slight variations in intensity these remained during the course of the experiment. When the animal was killed, degeneration was found in several nerves, especially in the branches of the left crural.

12. Dog. 15 injections in 31 days. In the course of the experiment, an abscess formed in consequence of the injections; this we opened. After the death of the animal, no nerve degeneration was found.

Thus, after infection by means of bacteria cultivated from the blood of a man, we observed in six out of seven rabbits, and in one of two dogs, a degeneration of the nerves. After infection by means of the same bacteria, obtained from the blood of a

rabbit which was attacked with a nerve degeneration, the degeneration was found in one rabbit, and in one out of two dogs. This bacterium in its form and the grouping of its cells, as well as in its behaviour whilst growing in agar-agar, presents some resemblance to staphylococcus pyogenes albus.

The growth on agar-agar was of a milky whiteness, and formed a somewhat thick bed with a shiny surface, and often with indented edges. When the growth has attained only slight thickness, it is somewhat transparent, with a slightly greenish tint.

The differences in sizes of the bacteria are more apparent than is the case in staphylococcus; these bacteria are generally larger than those in staphylococcus. When they float in the liquid they are often united in irregular groups, but very often merely in twos and twos. In one of the growths they had a tendency to take the form of streptococci, but this divergence disappeared little by little on continuing the cultivation. The bacteria easily absorb the colouring matters of aniline dyes, and if they be treated by Gram's process, the stain does not easily fade.

The development of the growth proceeds best at the temperature of the body; at a temperature of 20° centigrade it is somewhat feeble, and it almost entirely stops at a temperature below 15° centigrade. This micrococcus resists drying very well. Some little pieces of filter paper and some threads of silk, soaked in broth cultures, and then dried over sulphuric acid, at the end of several months developed new growths when they had been placed in a favourable medium. Naturally it was impossible to come to any conclusion from the variation in size of the different cells, or from the intensity of the aniline colours absorbed. The power of resistance against drying and corrosive sublimate was not found greater in the old growths than in those 20 hours old. If then there is amongst these bacteria a form capable of more resistance, it ought to present itself soon, at least in cultivations in broth.

*a.* Upon potatoes, this bacterium develops moderately well, but in a much less perfect manner than the staphylococcus albus. *b.* In a broth rendered slightly alkaline the development is good, if at least the bed of liquid be not too thick, the development proceeding much better on plates than in tubes. The micrococci fall at once to the bottom of the vessel, and do

not increase until they receive a sufficient quantity of oxygen. Thus it is that in cultivations by stabbing the medium scarcely anything is developed in the canal of the prick, whilst at the surface of the jelly a bed of milky whiteness is seen to extend. *c.* If the culture by pricking be made in nutrient gelatine, a narrow funnel is lightly formed on the surface, terminating by a rounded end in the canal of the prick, so that it appears as a little turbid spot in the lower layer of the gelatine.

Sometimes a turbid liquid is found in the funnel-shaped growth; at other times it contains air, according as the gelatine becomes liquid more or less quickly, and as the drying, which depends as well upon the temperature at which the growth is made as upon the composition of the jelly, operates more or less rapidly. The rate at which the gelatine is liquefied in the same jelly, and at the same temperature of cultivation, is always slow, but it is not always equal. In the growths on plates, the round opaque colonies, presenting a granular aspect when slightly magnified, are sometimes found in a depression of transparent gelatine; at other times they are surrounded by a white ring, perfectly circular, leaving between it and the colony a clear space; at other times, again, they are surrounded by a turbid border, white, and of a circular form, which touches the outer rim of the colony. If new cultures be made on plates with any one of these three varieties, the same forms are almost always found again.

The cohesion of the growth on agar-agar generally increases a little with the faculty of rendering the gelatine liquid. Sometimes the micrococcus leaves the gelatine quite solid. Some silk threads which had been soaked at Batavia with a pure broth culture of the micrococcus, which liquefied the gelatine, were dried afterwards over some sulphuric acid and carried to Europe in sterilized tubes. The cultures obtained therefrom produced micrococci which in every respect resembled those we have described, with the difference that they did not render the gelatine liquid. Some following generations of the micrococci, however, liquefied the gelatine, sometimes very slowly, sometimes rather quickly, and this variation could not be solely attributed to dirt or contact with foreign matter of any sort.

When the micrococcus which does not liquefy the gelatine is cultivated in some broth, and when this growth is left to itself for some time, it changes into the variety which liquefies the gelatine. Some cultures on plates prove this. Several tubes charged with broth were inoculated each with a colony which did not liquefy the gelatine. These tubes were exposed during a couple of days to a temperature of 25° centigrade, and then kept at the ordinary temperature. From time to time the culture on one of these tubes was taken to sow on a plate preparation. For some days these tubes only produced colonies which did not liquefy the gelatine; but those which were not opened until they had been kept twelve days or longer, produced colonies of micrococci which did liquefy the gelatine. These colonies were numerous in proportion to the length of time for which the growth had been kept, but all did not liquefy the gelatine equally quickly, and they presented the difference we have just described. In all other respects the growths were the same as regards their form, size, and the grouping of the cells, in looking like growths on a solid nourishing soil, and in the need that the bacteria had of free oxygen. In addition, experiment showed that they had retained the faculty of producing degeneration of the nerves in some rabbits. Two rabbits were sent to the pathological laboratory of Utrecht, in a large box, in which was emptied every day a diluted growth of these micrococci which did not dissolve the gelatine. One of the two died at the end of three months, probably of the violent cold to which the animal had been exposed. Only one nerve, a muscular branch of the right crural nerve, presented signs of very advanced degeneration; so great was the degeneration, however, that the number of fibres affected was quite four times as great as that of the normal fibres; in several other nerves also a slight degeneration was found. The other rabbit was killed after having passed two months in the infection box. A few degenerated fibres were found in a couple of nerves, but not more than might have been found in healthy rabbits.

Three other rabbits were put in another box placed in a heated chamber. The under surface of the lid was covered with a piece of wollen stuff, on which an agar-agar culture, suspended in water, was emptied every day, and sometimes a

broth culture of bacteria which did not liquefy the gelatine. As soon as the piece of stuff was dry, the bacteria were able to spread in the air of the case, a thing we assisted them to do from time to time by tapping the lid. We made certain that there was a crowd of bacteria in the air of the case, by placing a plate covered with a thin layer of peptonised broth thickened with agar-agar, and by rapping a couple of times on the lid. A few moments afterwards the plate was taken away, covered, and placed in the warm chamber; the following day the jelly was seen to be covered with crowds of colonies, amongst which the white colonies of the micrococci predominated. Of these three animals one died speedily without any assignable cause. In this animal nothing was found except here and there a degenerated fibre, such as might be met with in a rabbit in the normal state. The second rabbit was killed after having lived three months and a half in the infected surroundings that we have described. Latterly it became lean and its movements visibly slow. Of the nineteen nerves of this animal which we examined, eight showed signs of degeneration, but they were very slight. The third rabbit was killed five months after the commencement of the experiment. Seven out of the sixteen nerves which we examined were in a state of degeneration, and the degeneration was advanced. In a muscular branch of the right crural nerve, which supplies the extensors of the leg, a fourth part at least of the nervous fibres were in different phases of degeneration, while in the right external popliteal nerve about twenty-five degenerated fibres were found.

The only difference between these micrococci and those which were used in the experiments in the East Indies consisted in this, that the latter dissolved the gelatine slowly, and that the former were variable in their power of liquefaction. Once for all then it may be said, that the apparent difference in the power of micrococci to liquefy gelatine is of no importance as a differential feature. With this fact prominently before us, it becomes apparent that in the eight cultures derived from the blood of beri-beri patients mentioned above, the attention paid to the fact that two did not liquefy the gelatine, whilst six did do so, was a futile consideration. We remarked nothing concerning the pathogenic peculiarities, either positive or negative,

of these two growths. It is true that we succeeded in inoculating with one of them a rabbit, and a guinea pig, but the inoculation of the rabbit was made at Atjeh, where there was another rabbit which remained exempt from nerve degeneration, in spite of repeated injections with micrococci which dissolved the gelatine.

In guinea pigs we never succeeded in producing any nerve degeneration by infection. Two guinea pigs were kept forty-four days exposed to infection. They were shut up in a case, in the air of which a broth culture, greatly thinned with water, or a growth of agar-agar suspended in a great deal of water, was discharged each day by means of a pulveriser. The micrococci were of the variety which dissolved the gelatine. At the end of 44 days the animals were in perfect health, and did not present the least trace of nerve degeneration. This was the case in spite of the fact that the blood drawn immediately after death, and with all possible precautions, from the right ventricles of the heart, showed growths of the same micrococci that had been introduced into the cage containing the guinea pigs.

If, then, in the Indies the inoculations of micrococci not dissolving the gelatine have been made without results on a rabbit and on a guinea pig, it is no reason why we should refuse them any pathogenic properties, now that we know that micrococci exactly similar have produced a nerve degeneration in rabbits.

The property of dissolving the gelatine ought to be considered as of a secondary nature, as it appears that in eight out of fifteen cases, where cultures of bacteria have been made from the blood of beri-beri sufferers, a sort of organism has been obtained of such a nature as to produce a nerve degeneration in animals. This organism may be fairly considered as the cause of beri-beri.

In two other cases some white growths of micrococci were obtained which could not be studied very closely. Twice some yellow growths were obtained, which were sometimes met with by the sides of the white ones, and where the supposition that one was a variety of the other, was only combated by the conjecture, sufficiently hazardous, that in every case, when

we believed transition forms existed, there had been a pollution of the growths during manipulation. There remain only three cases out of the fifteen to be accounted for in which the cultures used for inoculation did not produce nerve degeneration in animals. The supposition is very probable that in these cases foreign organisms penetrated by accident into the tubes which had been inoculated with blood.

But even when we leave on one side these cultures, of the pathogenic value of which we cannot speak except with a greater or lesser degree of probability, it still appears to us of great importance that in six cases it has been possible to cultivate from the blood of beri-beri sufferers bacteria which, in four rabbits and two dogs, have been able to produce a degeneration in several peripheral nerves.

There is no doubt that in most of the animals which have served for the experiments the nerve degeneration ought to be considered as a pathological symptom.

It is true, as Mayer especially has shown, that a degeneration of nerve fibres may also be found in healthy animals, but this degeneration, physiologically speaking, is only present in a very restricted sense. If in a rabbit, immediately after it has been killed, the nerves are carefully removed and examined attentively, here and there a single degenerated fibre will be met with, but as a rule they are of a perfectly normal structure.

In our experiments the nerves were always isolated with a great deal of care, cut and fastened to small pieces of wood, such as matches for instance, hardened and coloured in a solution containing one per cent. of osmic acid, teased and examined in Canada balsam. Then the most minute nerve fibres could alone present any difficulty in the diagnosis of degeneration. We have never, however, admitted any pathological degeneration except when, even by a superficial examination, a certain number of degenerated fibres could be immediately recognised by their rounded lumps of myelin or some small and large dark globules.

We have inquired with the greatest care into the possibility whether the pathological modifications of the nerve fibres, upon the existence of which our preparations leave no doubt,

instead of being caused by an action peculiar to the micrococci cultivated from the blood of beri-beri patients, were not due to causes which had no connection with beri-beri. We could find no side issue by which such a result was even probable; there was nothing in the way these animals lived which could be taken into consideration. Our researches, made on some animals which served as a check, have shown us that the nerve degeneration could not be due to the manner of living.

The operation of injection was as simple and as short as possible. An assistant held the animal, and in a few seconds the injection was made in the abdomen, or under the skin of the back, never under the skin of the hind legs, where it was necessary to avoid any local lesion. Only one of these animals, a large dog, had to be tied up while the injections in the abdominal cavity were made, and this animal presented no symptoms of nerve degeneration.

The injections were often followed by suppuration, as well in the dogs as in the rabbits. It would, nevertheless, be wrong to attribute the nerve degeneration to suppuration, even of long duration. The animals used as checks in which suppuration was produced, on several occasions, by injections with other bacteria, did not present any nerve degeneration, and the only rabbit whose nerves resisted the influence of the micrococci (see above, No. II.) presented (appropriately) a certain number of abscesses, besides a purulent pleurisy. The strongest argument against the opinion of those who would consider the injection itself, or the suppuration resulting from it, as the cause of the nerve degeneration, is that this degeneration was also found in several rabbits which had lived in an atmosphere infected by these microbes, and where there was never any question of injection or of suppuration.

On the other hand, we have the case of a rabbit, in the jugular vein of which an agar-agar growth of staphylococcus pyogenes albus suspended in a neutral solution of sea salt was injected. The animal died on the fifth day, and presented some abscesses in the liver and kidneys, but it was only after we had searched for a long time in several nerves that a couple of degenerated fibres were found in a branch of the anterior crural nerve. The result of our researches is, then, that in our

opinion the micrococcus which we were able to cultivate from the blood of beri-beri patients is capable of producing in animals the characteristic symptom of beri-beri, namely, a degeneration of the peripheral nerves. In other words, that the micrococcus must be considered as the cause of beri-beri.

Now, is this micrococcus the only bacterium that can produce a nerve degeneration? We shall return to this question by and by. We will only say here that we have tried on three rabbits, and each time with negative results, injections with two forms of bacilli, which we obtained in our growths from the blood. We have not experimented with a third kind of bacillus, obtained from a beri-beri patient who had succumbed to acute pneumonia.

We further made experiments with micrococci found growing alongside of those which we have described in the growths from the blood of a beri-beri patient (see p. 112). Two male rabbits each received in 21 days sixteen injections of an oblong micrococcus (*a*), which in some growths became true rods but in others assumed a spherical form.

This micrococcus liquefied gelatine, and upon agar-agar took a yellow brown colour. During their lives nothing abnormal was noticeable in these aninals. In the smaller rabbit, which was also the weaker, after death a degeneration of nerves which seemed more than normal could be ascertained; in the other, nothing abnormal was found. In a rabbit during 14 days, 13 subcutaneous injections were made of a growth of large micrococci (*b*) of the tetrad form, which liquefied the gelatine and formed a citron yellow layer on agar-agar. No nerve degeneration was found in this animal.

Another rabbit during 15 days received 13 injections of a micrococcus (*c*), which was very like micrococcus (*b*), but which was distinguished from it by being developed on agar-agar, and by a feebler tendency to form tetrad groups. Again no nerve degeneration was found in this rabbit.

Lastly, a fifth rabbit in 14 days received 12 subcutaneous injections of a micrococcus (*d*), which differed from the two preceding in the fact that it was of a little paler colour, and in possessing a singular inequality in the size of the different cells, otherwise it resembled (*c*). In this animal there was no nerve degeneration found.

We give these experiments only in order to be more complete. We acknowledge that they do not prove that a pathological value cannot be attributed to the micrococci employed; especially as the slight degeneration met with in the rabbit injected with (*a*), ought to be considered as a proof to the contrary. It is very possible that if the animals had been exposed longer to the influence of these micrococci, the nerves might have become diseased, but as we had not time to continue these researches we cannot speak positively as to this. We can only state that the white micrococcus, which is most frequently met with, causes degeneration of the nerves.

From the blood of infected animals, we have on several occasions made cultures of micrococci similar to those which had been introduced into the body of the animal; upon one occasion, even 20 days after the last injection. Besides, by the side of the white micrococci of the blood, we sometimes saw others develop of a citron yellow and yellow brown colour, just as happened with human blood. In the case of living animals, the blood was obtained by making an incision in the ear by means of a scalpel which had been heated to redness a few moments before. The ear had been previously washed with soap and water, then shaved, disinfected with corrosive sublimate, and finally washed with alcohol. In the dead animal the blood was taken immediately after death from the jugular vein, or from the right ventricle of the heart; on the exposed vein or ventricle an eschar was made by means of a glass button strongly heated; then through the eschar the tapering and closed point of a small glass tube was introduced, whilst the proximal end was closed with some wadding. The point was pushed onwards into the cavity containing the blood, and then broken off. As soon as there was enough blood in the tube, a result which was facilitated by exhausting the air at the other end by suction, the tube was withdrawn, care being taken that it did not touch any part of the dead body except the eschar. Immediately afterwards some drops of this blood were placed in the tubes containing the nutrient jelly.

With the blood of two guinea pigs, which had lived in a case infected with the white micrococci, we cultivated, as we have above stated, the same micrococci. This did not succeed

with the blood of the rabbits which had lived in analogous conditions, although these animals were attacked with nerve degeneration.

If one considers that, relatively speaking, we have rarely succeeded in cultivating any bacteria from the blood of a man attacked with beri-beri, this negative result is nothing unexpected. In the majority of the rabbits, the temperature in the rectum was observed every day during several days before the experiments, and whilst the experiments were going on. No elevation of the temperature beyond the normal was observed. This temperature generally varied between 39·5° and 40° C.; once only a temperature of 40·6° was observed, a temperature which had also been noticed in an apparently healthy rabbit before it had received any injection.

# CHAPTER XVII.

## OF THE PRESENCE IN THE AIR OF BACTERIA WHICH CAN PRODUCE DEGENERATION OF THE NERVES.

It became imperative for us to establish the fact, whether or not it were possible to find in the atmosphere, in which beri-beri is endemic, any organisms capable of producing a multiple nerve degeneration. As a matter of fact, we found both inside and outside the barracks at Atjeh and Kola Radja some micrococci which in their form, their size, the disposition of their cells, and the behaviour of their cultures on a solid base, resembled the cultivated white micrococcus taken from the blood of those suffering from beri-beri. Some liquefied the gelatine, others did not.

Nevertheless, we have only been able to make but very insufficient researches into the pathogenic properties of these bacteria. This is a deplorable gap, but when we reflect how long a time elapsed before we arrived at the stage in our investigations, at which we even began to suspect that the cause of the disease might arise from microbes, it is not wonderful that so much was left undone.

A rabbit in thirty-one days received thirteen subcutaneous injections of a white micrococcus, which did not dissolve the gelatine, and which was obtained from the air of a room in a fort, Lamreng, in an infected district.

After it was killed, a nerve degeneration in the hind legs was found, especially in the upper branches of the sciatic nerves. This experiment, however, was not very satisfactory, because, in the preceding month, this rabbit on several occasions had received some subcutaneous injections of broth cultures of large bacilli, with pecular motion, obtained from the air. However, we had not found any reason for attributing to these bacilli any pathogenic properties

Some cultures of another white micrococcus, which liquefied the gelatine and altogether resembled that from the blood, we injected into a rabbit and a dog. The animals presented no nerve degeneration, nor any other symptom of disease.

In order to ascertain by experiment whether there was any foundation for the hypothesis that an infectious principle, capable of producing the disease, is found in the air of the places where beri-beri is endemic, we followed another plan.

In a barracks at Weltevreden, where latterly the recruits had often been attacked with beri-beri, a gas meter was placed in such a manner that the wheel could be moved by a weight and so suck in the air. This aspirator communicated with a small retort containing a weak sterilised solution of sea salt. Through the cover of the retort were passed two tubes, forming a Müller's valve. When the wheel of the meter was made to revolve, the air of the room passed slowly through the solution of salt, so that the bacteria floating in the air were to a great extent retained by the liquid. The meter showed the exact quantity of air consumed in the experiment. The solution of sea salt, charged with dust of every kind, and consequently also with bacteria, was afterwards injected into the abdomen of an animal. Now, if this animal suffered from degeneration of the nerves, it might be admitted that the cause of the degeneration existed in the air of the barracks. Two rabbits and a dog were treated in this way. In the case of the first rabbit, during seven days 35 cubic centimetres of chloride of sodium solution, through which 580 litres of air had passed, were injected. Upon the morning of the seventh day the rabbit was found dead, but still warm, in its hutch. The autopsy was immediately made. Some filaments of fibrin were found in the abdomen. No liquid was present in the cavity of the abdomen, nor the least trace of inflammation of the peritoneum. The pericardium contained a considerable quantity of clear serous fluid. A degeneration of recent date was found in several branches of nerves; the upper laryngeal nerve was rather far advanced in degeneration, the presence of degeneration in the cardiac branches of the vagus was doubtful; the great number of fine fibres normally present in this nerve, makes it difficult to judge of degeneration unless it be very great.

A rabbit, taken from the same hutch and placed in another case, died during the experiment on the first rabbit without known cause; it had not been used for any experiment. No signs of nerve degeneration were found upon it.

A second rabbit received in the abdomen, in the course of twenty-four days, some injections from a solution of sea salt, through which 1400 litres of air had passed. When the animal was killed, some recent filaments of fibrin were found between the intestines; the peritoneum otherwise appeared perfectly normal; the pericardium contained the normal quantity of serum. In addition, some hæmorrhages were found, here and there, between and in the muscles, especially of the posterior extremities. The nerves of the hind legs presented a feeble degeneration, but undoubtedly of a pathological nature.

On a large dog, during twelve days, several injections were made in the abdomen with a solution of sea salt, through which had been pased 36 cubic metres of air. The animal remained perfectly healthy, and after it had been killed, not only was no nerve degeneration found, but there was not the least indication of peritonitis.

We attempted, but in vain, to find by means of a plate culture from the solution of sea salt, charged with bacteria, the white micrococcus that we knew so well. However, we were only able to devote a short time to these researches, and it will be easily understood that a somewhat careful examination of a liquid, which contained a crowd of inferior organisms, required much more time than we were able to give to it.

From this solution of salt we cultivated micrococci, which were distinguishable from the preceding by a more elongated form, and a greater transparency of the agar-agar culture. One rabbit, which received twelve injections in fifteen days, presented no symptoms of nerve degeneration. But what appeared to us to be more important was, that, from the blood of the first rabbit, which was found dead, though still warm, in its hutch, after two injections, micrococci, exactly similar to the white micrococci obtained by culture from human blood, were cultivated. Later on, nerve degeneration was produced, by these micrococci, in a dog and a rabbit (see p. 120). It is very plain, that other elements besides micro-organisms were con-

tained in every fluid used for injection. Most notably might gases of a poisonous nature be dissolved in the fluid, and introduced into the system. It is open to discussion that a gaseous poison might be contained in the air of the barracks, and cause beri-beri in rabbits, with all the train of symptoms dependent upon nerve degeneration; but then it must be assumed that in every case the bacteria injected with the poison perished, or, remaining dormant for a time, revived when the symptoms of the disease developed. But, seeing that from the blood of this animal a culture of micrococci was obtained, which exactly resembled, in all respects, that which was cultivated six times from the blood of a beri-beri patient; and as also, in the rabbit, a degeneration of the nerves will be met, shown to be the principal pathological change, no deduction can be drawn from this result, except that bacteria, from the air of the barracks, possessed these pathogenic properties, and that they were certainly in such a condition as to multiply in the blood, and to produce a nerve degeneration, in this case in a rabbit, as they had also given beri-beri to the men who inhabited these barracks. These bacteria must have destroyed, or at least have thrown into the background the other living germs which had been injected with them into the abdomen. If our way of looking at it be correct, the organism of the rabbit had been the means of isolating certain micro-organisms floating in the air of the barracks, which were capable of producing beri-beri.

# CHAPTER XVIII.

## CONCERNING THE ORIGIN OF BERI-BERI, EXAMINED WITH REFERENCE TO THE PROPERTIES OF THE CULTIVATED MICROCOCCUS.

WHAT we have said seems to authorise us to admit that beri beri is caused by a micrococcus which exists in the places where the disease prevails, and which can penetrate into the human body.

It is very probable that this micro-organism enters by the organs of respiration with the air inhaled, and that from them it penetrates into the circulation. What proves this, up to a certain point, is the presence of nerve degeneration in some rabbits whose hutches had been infected with the micrococcus cultivated from the blood.

It is true that these bacteria are found in the organs of digestion, as well as in those of respiration; but it is not likely that the micrococci could penetrate into the blood as easily by the organs of digestion as by the lungs. In the stomach they come in contact with the hydrochloric acid secretion, and could with difficulty resist its influence. To prove this, some silk threads, or some pieces of filter paper, impregnated with a broth culture of micrococci, were dried over sulphuric acid and allowed to digest for some time in diluted hydrochloric acid. After removal they were washed with sterilised water, and placed in an agar-agar medium.

Some paper which had been so digested for fifteen minutes in a solution containing a thousandth part of hydrochloric acid remained completely sterile.

Although one must admit the possibility that the micrococci, in spite of their slight resistance to the action of hydrochloric acid, might be able, under some circumstances, to traverse the

stomach without undergoing any changes, it is more than probable that the infectious substance, which floats in the air, enters the body especially by the way of the lungs; and that the micrococci which enter into the digestive canal are generally soon rendered innocuous.

Experience concerning the propagation of beri-beri in human beings seems rather to indicate an infection by the air inhaled than an infection by the œsophagus.

It has often been stated that beri-beri is caused by food, but no one has ever shown any connection between food and the genesis of the disease, except only in the sense that, amongst those who live in a place where beri-beri prevails, it is the worst nourished who are attacked. Better nourishment cannot altogether prevent beri-beri from declaring itself; and, on the other hand, in a place where beri-beri does not prevail, bad nourishment does not produce nerve degeneration. As far as we have been able to ascertain, no case has proved, or even rendered it probable, that the disease was caused by the use of food containing any micrococci which brought about nerve degeneration. Neither did we find any connection between the propagation of beri-beri and the use of water as a beverage. Amongst the bacteria which we found in the drinking water at Atjeh, we never came across the micrococcus which we cultivated from the blood of beri-beri patients. But what does appear certain is, the influence of locality on the presence of the disease. There are some buildings, certain prisons, and especially certain barracks and ships, where beri-beri always appears amongst those who spend any time in them.

There are certain districts where, as at Atjeh, a considerable number of those who stay in them for some time are attacked with beri-beri. Amongst these, it is not only the private soldiers living in the barracks who are attacked, but also, from time to time, officers living in detached houses. The fault cannot be laid at the door of the buildings, as many are roomy and perfectly fitted up, their surroundings leave nothing to be desired. These phenomena are explained, better than in any other way, when it is admitted that the bacteria which cause the disease enter the body with the air inhaled. This supposition has received a great degree of probability since it has been proved

that the air of barracks where beri-beri prevailed, as a matter of fact, contained bacteria which were able to cause a nerve degeneration in rabbits.

If this be so, the bacteria which are the cause of beri-beri ought to be able to develop like saprophytes outside the human body, in the districts where the disease is prevalent, and afterwards to disperse in the air. This dispersion can only be made when the dust is dry. The cause of beri-beri ought consequently to be able to resist dessication. As we have seen above, this is the case with the white micrococcus that we found. This dried organism has been able to be preserved for whole months without becoming incapable of producing new growths; in fact, has produced them as soon as the circumstances became favourable.

It could certainly live as a saprophyte, and grow well, on all kinds of nutritive substances, provided that it be supplied with oxygen in sufficient quantity, and that the temperature is not too low. In the tropical temperature prevailing in the plains, and even during part of the day in the mountainous districts, our micrococcus grows well. Its most vigorous growth takes place at about 37° centigrade, but at 25° C. it still develops fairly well. It is only below 20° C. that the growth becomes insignificant, and at 15° C. hardly any development in the growth is observed. That is why we were able to cultivate these bacteria here (Holland), and place them in the rabbit hutches in the laboratory without being afraid of spreading the disease. In the warm rooms our growth did not sensibly increase in the winter, so it was necessary to place them in the incubator. All this accords perfectly with the fact that beri-beri is a disease peculiar to warm countries, and not met with outside the tropics, except where the temperature is very high during a part of the year, as is the case in Japan, where the disease only occurs in the summer and autumn.

Humidity is necessary to the growth of bacteria, a circumstance which explains why the countries where the disease prevails on a large scale are damp countries, low lying for the most part, and where there is a heavy rainfall. It has been noticed that the disease has been most widespread in wet years. Thus it is that the dampness of the soil at Atjeh, the torrential rains, and

especially the inundations caused thereby, appear to have exercised a peculiarly unfavourable influence. The increase in the violence of the disease at the commencement of the month of February 1887, was preceded by violent rain and inundations in the months of December and January (See in plates XI. and XII. the track delineated; the progress of the disease in this year is shewn by the broken line). The humidity of the surface layers of the soil might be expected to influence the development of bacteria, because so long as humidity continues, the growth of bacteria favoured by the high temperature is luxuriant. When the rains have stopped, and the river has returned to its bed, the soil dries very quickly, and so gives the bacteria an opportunity of spreading on a large scale in the surrounding atmosphere. Where the land is steeply inclined, where the rain water runs off rapidly, and where the soil seldom remains soaked for long, even by the most violent rains, the chances of a great multiplication of bacteria are certainly less favourable.

In dwellings, however, especially in those inhabited by a large number of persons, the prisons, barracks, the normal schools for the native teachers, and on board ships, there is always plenty of food for the bacteria, upon which they fix themselves and increase; and when by the tropical heat they become dried and shrivelled, they are spread by the air. They may then enter human beings, or fix themselves anew on a damp place to again multiply. The great power of resistance possessed by the micrococci is sufficient to explain the transport of beri-beri from one place to another, even from land to sea. The bacteria can be carried from a building in an infected district by clothes or otherwise, and where they fall they easily find the conditions necessary for a new increase. These conditions do not appear to be always met with, even in districts that are hot and low lying. The military hospital of Padang is an example of this. Some thousands of beri-beri patients have been sent there from Atjeh, and it cannot be doubted that they have frequently carried the cause of the disease with them. Beri-beri, however, has not spread there, although the disease is not foreign to the place. Not only have there been epidemics of beri-beri at Padang, but we are assured that the disease at pre-

Neither is the disease propagated in the establishment for convicts suffering from beri-beri at Buitenzorg, although infection must be constantly brought in from outside, and although more than once beri-beri has broken out at Buitenzorg.

It is not at present worth while spending the time that would be necessary to explain these peculiarities. There are so many things to be taken into consideration that it is impossible to keep count of all, even for one who is perfectly acquainted with the local conditions.

These anomalies, however, are incapable of lessening the signification of the possibility of the transport of this disease which has been so often observed. Besides, it is known that in other diseases, such as cholera for example, the disease can generally be carried elsewhere, but not at all times or everywhere, without its being always possible to give a sufficient reason for this being so.

As we have said, infection ought always to be able to repeat itself, in order to manifest the disease; from this it must be concluded that in the human subject the disease meets with great resistance. It is necessary that a person should have lived for some time in a building or a district where beri-beri is prevalent before he is attacked with the disease.

Every exception to this rule that we have come across has seemed to us more apparent than real. In some instances it happened that persons who had only been one or two weeks at Atjeh were seized with the disease. In them beri-beri seemed to develop very rapidly, and symptoms of degeneration of some standing apparently could be ascertained to exist in the muscles and nerves. In all such cases careful inquiry betrayed the fact that they had suffered from beri-beri elsewhere to a greater or less extent, and that the rapidly developed symptoms were merely an aggravation of an old trouble.

Amongst the troops which are sent to Atjeh, endeavours are made to exclude all those who show even faint symptoms of beri-beri; but they have not always been successful; and with the great prevalence of the disease in the Netherlands Indian army, this will not be attained unless, in the inspection of the troops intended for Atjeh, a careful examination be made of the irritability of the nerves and muscles of the lower extremities.

The tendency to contract the disease is evidently augmented by the cause of the disease continuing to operate; at least those who have once had beri-beri show a great tendency to relapses as soon as ever they come into places where the disease prevails. But even amongst these the nerve degeneration generally only progresses slowly. From this we must conclude that the human organism presents a very strong resistance to the cause of the nerve degeneration.

This power of resistance is greater in women than in men, in infants and old men than in youths, in Europeans than in natives. In addition, it depends upon all sorts of circumstances, of which some can be controlled (bad food and excessive work, for example, seem to diminish it), but others are of a nature so complicated that we cannot at the moment give any explanation. It is enough to draw attention to this singular fact, that at Atjeh the Chinese, even the coolies, have remained almost without exception free from beri-beri, whilst experience has taught us in the most convincing manner that at Singapore, at Dehlí, at Banca, and at Billiton, the Chinese possess no immunity from beri-beri, either as a race or from their way of living. But if the reason for these differences in the resistance to the disease is still obscure, the fact that in general the cause of the disease does not easily gain ascendency over the human organism is perfectly in accord with what we have observed.

We regularly found bacteria in the blood of beri-beri patients as long as they remained in the places where the disease prevailed; but if the bacteria were not continually imported from outside, they quickly disappeared altogether from the blood. Even when the patients were not withdrawn from the infected country, the number of bacteria found in the blood still diminished rapidly when they were placed under more favourable circumstances. Thus the bacteria in the blood became daily fewer in those beri-beri patients who entered the spacious and excellent hospital of Panteh-Perak.

The presence of bacteria of irregular form and staining with difficulty so frequently met with, and the fact that we could not discover microscopically bacteria in any organ, support the opinion that the bacteria which have penetrated into the circulation of the blood have at first been able to multiply, but that

afterwards they have been obliged to succumb in the struggle. We have never observed the presence of phagocytes as adversaries of the bacteria. We have never found any micrococci or bacilli enclosed in the white corpuscles of the blood. Should later researches confirm our experience that the bacteria are not in a state to lodge themselves in the tissues, it is not likely that they should be combated by any phagocytes. It is more likely that these bacteria, while living in the human blood, produce some substances which, penetrating the tissues with the nutritive liquids, destroy the nerve fibres and at the same time kill the bacteria themselves. In order, therefore, to produce any considerable degeneration of the peripheral nerves, the bacteria would have to make a new invasion of the blood, and develop a fresh supply of poison. This supposition perhaps finds some support in the experience that we acquired in the culture of bacteria from the blood. In the greater number of cases the blood, spread on the nutrient jelly, remained sterile, although, with the assistance of the microscope, bacteria were to be found. The results were better when we no longer spread the blood over the jelly, but mixed it freely with the melted gelatine, so that it was well divided.

This appears to support the opinion that there are some substances in the blood antagonistic to the development of the bacteria, and that in simply spreading the drop of blood, these substances remained there in so great concentration that development became impossible. When the drop of blood was mixed with some broth, the result was not so favourable; this was probably because, like the micrococcus we cultivated, there was a great need of oxygen, a condition which could be better satisfied by spreading the gelatine with which the blood was mixed in a thin layer, than by placing the blood in a liquid where the bacteria fell to the bottom.

Several properties that the study of the disease forces us to attribute to the cause of beri-beri, are met with in the micrococcus that we cultivated from the blood of beri-beri patients. However encouraging this may be for researches in this direction, nobody knows better than we do that this is but the first step in the proper direction. In establishing the proof, it is desirable that the same micrococcus should be found

in the large majority of cases of beri-beri. It is true that to us it scarcely seems possible that the micrococcus producing nerve degeneration which we cultivated six times from the blood of beri-beri patients, and which was also obtained from the blood of a rabbit injected by a bacterial culture and suffering from a nerve degeneration—it seems scarcely possible to us, we say, that this micrococcus can be rejected as the cause of beri-beri. However, it cannot be undesirable to augment the number of observations. This is why we have learned with pleasure that van Eecke, without knowing anything of what we had found, has cultivated, from the blood of patients at the great establishment for beri-beri sufferers at Buitenzorg, two kinds of micrococci. One gives a milk white culture perfectly similar, as it appears, to ours; and the other shows cultures of a yellow citron colour, and resembling, according to the description he gives of it, the large micrococcus forming tetrad groups.[1] We shall hope soon to receive fuller communications on this subject from van Eecke, who is now sub-director of the Pathological Laboratory at Batavia.[2] It is also absolutely necessary to know whether the different forms that we, as well as van Eecke, have cultivated from the blood of those suffering from beri-beri, are not in fact, as we are inclined to believe, only varieties of the same species.

The history of bacteriology has only too often taught us how dangerous it is to consider several forms as belonging to the same species, without incontestible proofs of the variability of these bacteria. We must admit that we are not in a position to resolve this question, which is so highly important to the proper comprehension of the cause of beri-beri, or, at least, we cannot give any sufficient reasons for or against the specific difference of these micrococci. Yet another difficulty is intimately connected with this subject. We have found in the blood of beri-beri patients, in addition to the micrococci, bacilli, sometimes even (see Plate II., fig 1) almost nothing but bacilli, while from that blood we could only cultivate micrococci which exercised a pathogenic action.

Do these bacilli and micrococci belong to one family? Do

[1] Geneeskundige Tijdschrift voor Nederlandsch-Indië, vol. xxvii., p. 71.

[2] See also vol. xxviii., p. 145, of same periodical.

they form one species, of which the bacillus form is not susceptible of being cultivated, or can only be cultivated with great difficulty; or, on the other hand, are there several species of bacteria in the blood of beri-beri patients which may have the same pernicious influence?

There is not, *a priori*, any stronger argument to advance against this last supposition. If it be admitted that in beri-beri nerve degeneration is caused by a poison formed by the influence of bacteria living in the blood, the possibility must be admitted, that these different bacteria could produce the same poison or an analogous one. One would be justified in this supposition, not only because we have found several forms of bacteria in the blood, and were able to make cultures of various micrococci, but also because Ogata in Japan, and de Lacerda in Brazil, have described some bacilli which they cultivated from the blood of beri-beri patients, and which they considered to be the cause of the disease. In his detailed narrative, de Lacerda[1] makes mention of a transformation of cultivated bacilli from streptococci to diplococci and monococci, while he says he has met with micrococci in the blood as well, and shews some drawings of the same.

Further researches made with every care and with every possible exactitude could alone throw light upon these important questions.

Our knowledge concerning the presence of pathogenic bacteria in the air is also very incomplete. As we have said, we have obtained no evident result except in connection with the pathogenic action of a mixture of bacteria. We have scarcely been able to make any experiments with the micrococci cultivated simply from the air, which were similar to those obtained from the blood.

Some researches on a large scale ought, however, to be made in this direction, if it be wished to obtain a more precise idea as to the etiology and pathology of beri-beri.

[1] O Microbio do Beri-beri. Rio de Janeiro, 1887.

# CHAPTER XIX.

## AS TO THE MEANS OF COMBATING THE DISEASE.

HOWEVER great and important may be the gaps in our researches, we believe that our investigations have shown us how to combat the disease.

As to medicinal treatment, the study of the disease has made us understand the powerlessness of therapeutics, properly so called, in this affliction. We know of no means by which we are able to induce the degenerated nerves to take on regeneration; happily, however, the vis medicatrix naturæ assists in so doing.

When the number and importance of the destroyed nerve fibres are not too great, nature regenerates, little by little, what has been destroyed. The removal of the sick from a centre where they are continually exposed to new invasions of bacteria, and before it is too late, is therefore indicated, and in perfect harmony with the old experience, which teaches us that rapid removal into districts where beri-beri does not prevail, is the best means of bringing about a cure.

As to prophylaxis, the researches into the causation of the disease seem clearly to indicate the path to be followed. We have found that bacteria, proceeding from the air of barracks where beri-beri had broken out, could produce nerve degeneration in rabbits; and that from the blood of a rabbit infected with these bacteria, micrococci could be obtained, able to produce nerve degeneration in other animals. These micrococci, after various inoculations, were found to be exactly similar to the micrococci which, at Atjeh and Batavia, had been cultivated from the blood of those suffering from beri-beri. Therefore, what is required is plain. If one wishes to prevent the disease, it is necessary to destroy the bacteria which exist in the air. These

bacteria must develop in dwellings, or in the earth, or perhaps in both. If beri-beri prevail in a private house, a prison, a barrack, a hospital, or on board ship, it is necessary to attempt to rid the building or vessel of the bacteria found therein. It is necessary, therefore, to try to destroy all the bacteria that are present at any given moment. Immediately afterwards, it is true, new bacteria will come and establish themselves, but if the disease is really confined to this building, or this ship, no germs able to produce beri-beri will be produced. If, however, the disease, far from being confined to certain buildings, prevails throughout a whole district, it must be admitted that the noxious bacteria exist in a very large number in the soil. It would seem that dwellings are favourable places for their multiplication, so that very soon the air within contains more noxious bacteria than the air outside them. The destruction of bacteria in dwellings will then certainly be very useful, but it cannot be permanently effective, as will be seen presently. The pathogenic germs soon penetrate there again, and very shortly afterwards it will become necessary to repeat the disinfection. The result obtained can only be partial, because the cause of the disease remains; and, if it can be combated with good effect by the disinfection of dwellings, it cannot be removed from them completely. There are, then, two desiderata: the first is, destruction in the houses of the organisms which are the cause of beri-beri; the second, the purification of the ground from the same organisms.

The first had already been begun to be carried on before we commenced our researches.

Upon the solicitations of Cornelissen, Inspector of the Civil Medical Service in Java and Madoura, and upon those of the military medical officer, Dr Kobler, disinfection was practised at Atjeh, at the end of the year 1886. All the houses containing large numbers of men were disinfected with corrosive sublimate, and afterwards the disinfection was repeated every month on a smaller scale.

During the first disinfection the houses were washed from top to bottom with a solution of corrosive sublimate, and all the clothes of those living in the houses were treated in the same manner. Afterwards, every month, the floors, the skirtings, up

to a man's height, and the furniture, were washed with a solution of corrosive sublimate (1-1000).

It must be admitted that this measure did not succeed in making the disease altogether disappear from Atjeh, but beriberi greatly diminished in intensity there after this disinfection. The table we give proves this. (See Plates XI. and XII.) The unbroken line gives, for each group of persons, the progress of the disease for 1886, starting from the month of February; in the same manner the broken line indicates the progress during 1887; and the dotted line for the first six months of 1888. The lines are traced in such a way that the ordinates give the total of sick.

At the end of every month, the proportion of the beri-beri patients from each group was obtained by adding the numbers indicating the effective strength of the troops for each day of the month; then we multiplied by one hundred the number of beri-beri patients entered at the hospital during the month, and finally divided the product obtained by the sum of the effectives of each day of the month. Consequently, the proportion of the sick was obtained, as well of Europeans as of natives and convicts, independently of the changes in the effective force of the troops.

The disinfection commenced at the end of the year 1886, and it is remarkable to see how the number of sick diminished more and more during the first six months of the year 1887, except for a large increase in the spring, more especially amongst the natives. In the last months of the year 1887, and at the commencement of 1888, a fresh recrudescence of the disease was observed, which as the dotted line shows was again followed by an amelioration. During the twelve months of disinfection the number of cases was much less than that for the year when disinfection had not yet been practised. The mortality after the disinfection diminished in still greater proportion. It has been calculated for six consecutive months, in the same way that we did it for the cases of sickness, as a percentage of the effective force. Here are the totals:—

| | Europeans. | Amboinicans. | Natives. | Convicts. |
|---|---|---|---|---|
| January—July 1886 | 0·026 | 0·25 | 0·035 | 0·126 |
| July—December „ | 0·016 | 0·03 | 0·02 | 0.066 |

| | Europeans. | Amboinicans. | Natives. | Convicts. |
|---|---|---|---|---|
| January—July 1887 | 0·0007 | 0·003 | 0·02 | 0·06 |
| July—December „ | 0·0003 | 0·0002 | 0·004 | 0·01 |

There remains, therefore, no doubt that beri-beri considerably diminished at Atjeh after the application of disinfection. The state there was even more favourable than the figures show. In the latter year, the doctors decided more quickly than formerly as to the diagnosis of a case of beri-beri. The number of deaths especially fell considerably, as soon as the effect of the disinfection came into play at the end of 1886; it fell even still more than the figures show.

In order to know the entire mortality caused at Atjeh by beri-beri, it would be necessary to know the number of those who were sent to Padang, and who died during the voyage, or soon after their arrival at Padang. We have no exact returns as to this, but there is not the least doubt that the number was much greater in 1886 than in 1887.

In the months of June, July, and August 1886, months in which the lines show a comparatively small death-rate in proportion to the number sick, there died at Atjeh alone, 51 soldiers and 105 convicts from beri-beri; and in the same months of 1887, 13 soldiers and 4 convicts only. If one takes into consideration that, during this time, the total number of convicts fell from about 1000 to close upon 300, one will see that nevertheless the diminution was very considerable; and the figures would be still more favourable if one could add to them the deaths of those who were away from Atjeh.

We see then that, after the application of a regular disinfection at Atjeh, the sanitary state was improved, and if the complication of the question does not allow us to deduct from this an absolute proof, it is impossible to deny that the coincidence between the sanitary amelioration and the application of the disinfection must plead in favour of that measure.

Beri-beri, however, is endemic at Atjeh. One will never be able to combat the disease there with complete success while the earth remains unrelieved of the cause of the disease. Any radical measures to attain that end are impossible. One might, it is true, do much to assist the rapid and regular draining off of the waters, even during the heavy rains; earth cutting might

be restricted to the extent absolutely necessary, so as not to continually expose new surfaces of ground, which, being damp and rich in food for these bacteria, offer them a propitious soil for multiplying and afterwards spreading as dust in the air. It is considered probable that the disturbance of the soil is intimately connected with the presence in the air of the infectious matter of beri-beri as well as that of malaria. One knows generally, that marsh fevers augment in intensity, when earth cutting takes place in the places where malaria prevails. At Atjeh, beri-beri reached its highest point of intensity a short time after we had established our lines of concentration, for which it was necessary to execute in a short time a large amount of earth cutting. The redoubling of the intensity of the disease in the latter half of 1887, only declared itself after some very considerable works had been commenced, in order to protect the territory we occupy at Atjeh against inundations. It was to be supposed from what we have said above, that these works would lead to an aggravation of the disease, but this danger would be only of a temporary nature, and should be more than compensated for by the permanent utility of the improvement in the embankments of the river. Besides, the aggravation was not so considerable as the lines indicating the progress of the disease show, seeing that other unfavourable circumstances, during the last months of 1887, might be taken into account.

It was only amongst the convicts that the increase of cases became considerable in the month of December 1887. The number of those attacked, in proportion to the effective strength, was large, although the total of the mortality was really small. Besides, it must be remarked that the number of sick among the convicts generally presents greater fluctuations than amongst the military. This is probably owing to the fact, that beri-beri is a very widespread disease amongst the convicts in Netherlands India, and that amongst those who are sent to Atjeh, the likelihood that there may be some who have already suffered from the disease, or who, having the disease upon them, develope it only after admission to prison, is much greater than amongst soldiers.

However difficult a task it may prove, not only to put

limits to the disease, but to combat it in any district where it prevails, we have reasons for believing that it can be stamped out when it is confined to particular buildings.

If the conclusions drawn from the results of our researches are correct, the disease ought to disappear after a careful disinfection of a building infected by beri-beri. The danger that, after the disinfection, the micrococci of beri-beri will enter anew with the air, in a neighbourhood where the disease is not prevalent, is chimerical. The only danger is that infection may re-enter with clothes or other things brought from the districts or dwellings where the disease is endemic. The question whether, in this disease as in cholera and abdominal typhus, the patient himself is to be considered as a focus of infection, ought, it would appear, to be answered in the negative.

We have been obliged to conclude from our bacteriological examination of the blood, that the infectious matter only increases in the blood during a relatively short time, to be very soon destroyed, if not altogether, at least to a great extent. Had the beri-beri sufferer, in his body, even a crowd of bacteria, it cannot be admitted that he is able to disperse them except under accidental circumstances, which, as far as this question is concerned, have only a very secondary signification.

In beri-beri patients with intestinal hæmorrhages, arising perhaps from dysentery, or from wounds made by the *anchylostoma duodenale*, which we have never searched for in vain in the intestines of natives, some micrococci of beri-beri might also escape with the blood.

In general, however, there is no reason for admitting that the ordinarily healthy intestine of a beri-beri sufferer is in a state to emit bacteria with the stools.

The kidneys can still less be supposed to be the means of transfer, because, although we have often found fatty degeneration and some symptoms of congestion in the kidneys, we have never found any destruction of the tissues. Exanthem and desquamation of the skin and expectoration of bronchial mucus are scarcely met with in beri-beri.

To all this it must be added that bacteria are no longer met with in the blood of a beri-beri patient a few weeks after he has left the place where the disease prevails.

According to us, therefore, there is not much danger of a person suffering from beri-beri carrying the disease from one place to another, provided that care be taken that his clothes and everything that he takes with him from the contaminated locality be properly disinfected. The manner in which this disinfection is to be carried out for buildings, furniture, and clothes, cannot always be the same.

Whenever a current of steam can be employed, this is the best means of killing the bacteria. For buildings and for furniture generally this means would not be applicable, and it is then necessary to make use of a substance dissolved in the water which has the property of destroying the bacteria. Amongst these substances corrosive sublimate ought first to be taken into consideration, as it is the most active.

After a thorough sprinkling with a solution of corrosive sublimate, the whole is well washed with water, in order to remove the corrosive sublimate. Our experience at Atjeh has taught us, there is no reason to fear that the people living in the houses disinfected in this way will show any symptoms of mercurial poisoning. Wherever it is possible, we recommend the employment of a solution of that mercurial salt, which contains besides a free acid. Like other bacteria, the micrococcus of beri-beri is more rapidly killed by a solution of corrosive sublimate that contains some tartaric or hydrochloric acid than by a neutral solution.

Some pieces of filter paper, impregnated with a broth culture of micrococcus, and then dried over sulphuric acid, have to remain at least five minutes in a solution of corrosive sublimate of 1-5000 in order to be sterilised; while one or two minutes in a similar solution, but containing in addition 0·5 per cent of tartaric or hydrochloric acid, suffice to completely disinfect the paper. An immersion for fifteen seconds in a solution of the following composition killed the micrococci:—$Hg\ Cl_2$ 1 part, HCl 5 parts, $H_2O$ 1000 parts.

Of course some things which have to be disinfected cannot stand contact with hydrochloric or tartaric acid. Besides, it is not always possible to sprinkle buildings and things with a solution of corrosive sublimate in such a way as to destroy all the living germs. This is especially the case in the East Indies,

where so many erections are built of bamboo and similar materials, which can scarcely be thoroughly disinfected unless they are burned down.

To apply disinfection properly, directions with regard to it must be given according to circumstances. A sufficient disinfection, especially of buildings and ships, entails not only great expense, but exacts also great self-sacrifice and a scrupulous exactitude in the employment of means; but this is not too much to insist upon when fighting a disease that causes such ravages as beri-beri.

Our researches lead us to hope that disinfection, at least if properly applied, can not only restrict beri-beri within the narrowest limits, in places where the soil contributes to the propagation of the cause of the disease, but can also cause it to completely disappear when it is confined to a few buildings.

# DESCRIPTION OF THE PLATES.

## PLATE I.

Photograph of two beri-beri patients. The one to the left is a type of dry beri-beri. The other is a type of wet beri-beri.

## PLATE II.

Fig. 1. Blood of a beri-beri patient (European). Preparation stained with fuchsine. Between the blood corpuscles are a crowd of bacteria, of which the majority are only coloured at the extremities. Here and there a few micrococci. Zeiss. Homogeneous apochromatic immersion, 3/1.40, Oc. 12.

Fig. 2. Blood of another beri-beri patient (native convict). Preparation with fuchsine. Micrococci and bacteria of different sizes. Zeiss. Homogeneous apochromatic immersion, 3/1.40, Oc. 12.

Fig. 3. Nerve fibres from the phrenic (Autopsy, No. 35). Recent degeneration. The medullary sheaths of the two fibres marked (*b*) have coagulated in masses. The degeneration of the other nerve fibres is of older date. At (*c*) is seen a transition between degeneration in masses and a later phase. A fibre almost intact is shown at (*a*). Leitz. Obj. 5, Oc. 3.

Fig. 4. Degenerated nerve fibre of the recurrent laryngeal nerve (Autopsy, No. 33). The medullary sheath is coagulated in masses. *a*. Ranvier's nodal points. *b*. Interannular nucleus. Leitz. Obj. 5, Oc. 3.

Fig 5. Degenerated nerve fibre of the external popliteal nerve (Autopsy, No. 14). The coagulated masses of the medullary sheath have almost wholly disappeared. There is at

(*a*) a fusiform thickening, where a certain number of myelin masses are to be found. Otherwise, Schwann's sheath has collapsed round a lump of reddish grey, where a large number of nuclei are seen (*b*). Leitz. Obj. 5, Oc. 3.

Fig. 6. Degenerated fibre of a motor nerve leading to the common extensor of the fingers (Autopsy, No. 29). Similar fibre to the foregoing, but seen with a higher power. Some nuclei (*b*), the descendants of the interannular nucleus, exist in the middle of a lump resembling foam. Again, here and there between these nerve corpuscles a globule of myelin is met with (*a*). At different distances from each other spindle-shaped thickenings of the fibre are found, the fibre being in the phase of mucoid degeneration. The contents of the nerve fibre, as much as are not composed of frothy mass, are characterised by a fibrillar structure. Two or three, or sometimes more, small fibres are contained in Schwann's sheath. Leitz. Obj. 8, Oc. 3.

Fig. 7. Degenerated fibres of the external popliteal nerve, branch to the anterior tibial muscle (Autopsy, No. 29). A nerve fibre (*a*) is found in the phase of frothy degeneration. Another fibre (*b*) has not suffered, or has been regenerated. At the side are found a number of other fibres, very fine (*c*); of which some have a medullary sheath, extremely small; whilst others, looking like fibrils rich in nuclei, but without distinct medullary sheaths, occupy the place of the nerves. The richness in nuclei is very great. Leitz. Obj. 8, Oc. 1.

Fig. 8. Regeneration of an extremely fine fibre of the external popliteal nerve (Autopsy, No. 7). Between two segments (*b b*), which although very small have evidently a medullary sheath, is found a nucleated segment (*a*) without medullary sheath. Leitz. Obj. 8, Oc. 3.

Fig. 9. Regeneration of a fibre of the external popliteal nerve (Autopsy, No. 7) *b*, *b*. Segments with medullary sheaths; *a*, intervening part, also possessing a medullary sheath; *c*, the nucleus of the intervening part; *d*, myelin globules. Leitz. Obj. 8, Oc. 3.

Fig. 10. Regeneration of fibres of the external popliteal nerve

(Autopsy, No. 71). The intervening part is here composed of three segments. Otherwise like Fig. 9. Leitz. Obj. 5, Oc. 1.

Fig. 11. Degeneration of fibres in a small nerve branch met with on the surface of the heart (Autopsy, No. 35). *a*, Thick fibre, intact, with a medullary sheath; *b*, small fibre, intact; *c*, small fibre, degenerated; *d*, fibres of the great sympathetic, without medullary sheaths. Leitz. Obj. 8, Oc. 1.

## PLATE III.

Fig. 1. Transverse section of the first anterior sacral root (Autopsy, No. 29). This root is almost intact. Leitz. Obj. 3, Oc. 1.

Fig. 2. The same transverse section seen under a much higher power. Several swollen axis cylinders are seen. Leitz. Obj. 8, Oc. 3.

Fig. 3. Longitudinal section of the same root. Slight bead-shaped swelling of fibres. Leitz. Obj. 8, Oc. 3.

## PLATE IV.

Fig. 1. Transverse section of the radial nerve (Autopsy, No. 9), treated by Weigert's method. Only one bundle is drawn. A large number of its dark fibres have disappeared. Leitz. Obj. 5, Oc. 1.

Fig. 2. Transverse section of a peroneal nerve (Autopsy, No. 29), of which we have given the anterior sacral root in Plate III., figs. 1 and 2, treated by Weigert's method. Loss of nerve fibres very considerable; *b*, intact nerve fibres; *c*, blood vessels; *d*, epineural covering; *e*, perineural sheath. Leitz. Obj. 5, Oc. 1.

## PLATE V.

Fig. 1. Section of the same nerve, from a preparation coloured with picro-carmine; *α*, *α*, nodules described by Rosenheim and others. Leitz. Obj. 3, Oc. 1.

Fig. 2. Section of a cutaneous branch of the sciatic nerve (Autopsy, No. 29). Prepared with picro-carmine. Loss of nerve fibres. Leitz. Obj. 5, Oc. 1.

## PLATE VI.

Fig. 1. Section of peroneal nerve. Leitz. Obj. 8, Oc. 3.

Fig. 2. Section of a terminal branch of the anterior crural nerve. Leitz. Obj. 8, Oc. 1. Both taken from the same subject (Autopsy, No. 29), of which we have given a drawing of the first sacral root in Plate III., figs. 1 and 2. The majority of the fibres have disappeared, and the place that the nerve fibres occupied is taken up by a cavity surrounded by a solid interstitial tissue. Here and there in *a a* there are still some fibres intact. In some fibres the cavity is filled by a swollen granular mass. Sometimes the contents can be recognised as a swollen axis cylinder; (*b*) sometimes as a granular mass that we cannot otherwise define.

Fig. 3. Transverse section of diaphragm (Autopsy, No. 9). Prepared with alum-carmine solution; *a*, fibres greatly swollen with proliferation of nuclei. Leitz. Obj. 8, Oc. 1.

## PLATE VII.

Fig. 1. Isolated muscular fibres of the gastrocnemius (Autopsy, No. 29). Fibre swollen in spindle-shape form. At the swollen part the transverse striæ have disappeared and the number of nuclei have increased. Leitz. Obj. 8, Oc. 1.

Fig. 2. Muscular fibre of the gastrocnemius (Autopsy, No. 29). Atrophied muscular fibre with proliferation of nuclei; the transverse striæ have become indistinct in places. Leitz. Obj. 8, Oc. 1.

Fig. 3. Transverse section of the spinal cord at the level of the commencement of the sciatic nerve (Autopsy, No. 29). Preparation treated by Weigert's method. It can scarcely be doubted that here there is a slight loss of fibres in the posterior radicular zone. Magnified 20/1.

## PLATE VIII.

Fig. 1. Diverse nerve cells, obtained from carmine preparations of the same spinal cord: *a*, normal nerve cell; *b*, *c*, cells with vacuoles; *d*, *e*, cells in which the nucleus is placed against the cell wall, and with accumulation of pigment. Leitz. Obj. 8, Oc. 3.

Fig. 2. Transverse sections at different heights of a spinal cord, in the posterior columns of which some modifications were found (Autopsy, No. 24). (*a.*) Section of the spinal cord at the root of the fourth lumbar. Degeneration of the root and of the radicular zone, also of the posterior column on both sides. (*b.*) Section of the spinal cord a segment higher. The radicular zone is still in a state of degeneration on both sides. (*c.*) Section of the spinal cord at the next segment. (*d.*) Section of the spinal cord at a higher segment.

In *c.* and *d.* the place of the secondary sclerosis in the posterior column is indicated by a dark spot. This gets nearer and nearer to the median fine.

(*e.*) Section of the upper part of the dorsal region of the spinal cord. The spot of degeneration has reached the median fissure. (*f.*) Section of the lower part of the cervical enlargement. Signs of degeneration can still be seen here. Enlargement by magnifying glass.

## PLATE IX.

Fig. 1. Section of a posterior lumbar root (Autopsy, No. 42), between the ganglion and the spinal cord. The fine fibres are in the majority in this root, and are a little more numerous than in the normal root. Leitz. Obj. 8, Oc. 1.

Fig. 2. Section of the same posterior root, between the nerve trunk and the ganglion. Leitz. Obj. 8, Oc. 1. In this section some large fields of atrophied fine fibres are met with.

Fig. 3. Section of a muscular branch of the recurrent laryngeal nerve (Autopsy, No. 33). (*a*, *a*) Spots where some small degenerated fibres occupy almost the whole surface of the section, coloured red with carmine.

Fig. 4. Section of a normal vagus nerve taken from a patient affected with paralytic dementia, to show the distribution of the fibres into large and small groups. Leitz. Obj. 5, Oc. 3.

## PLATE X.

Section of the vagus nerve of a beri-beri patient (Autopsy, No. 31) where the number of fine fibres has considerably increased. Leitz. Obj. 5, Oc. 3.

## PLATES XI. AND XII.

Charts showing the progress of beri-beri at Atjeh. The ordinates indicate in hundredths the proportion of persons who have been attacked by the disease. In order to prepare this table, the number of beri-beri sufferers admitted in the course of each month to the hospital at Panteh-Perak, and at the naval stations, has been multiplied by one hundred, then this number has been divided by the sum of the numbers indicating the real effective force for each day of that month.

For example, in the month of March 1886, 306 European soldiers entered the hospital suffering from beri-beri, whilst the sum of the numbers, indicating for each day of this month the effective force of European troops, was 68,710. The figure indicating the proportion of the sick, is then given at the end of March as 0·45 per cent. The crosses show the period of the commencement of the process of disinfection.

The number of convicts had greatly diminished in the later months of the year 1886. In August of this year (1887) the average number was $\frac{28752}{31}$, in September $\frac{26128}{30}$, in October $\frac{12134}{31}$, in November $\frac{7800}{30}$, to remain afterwards at about the same proportion. Besides, they were lodged in other buildings, and their old huts were burned.

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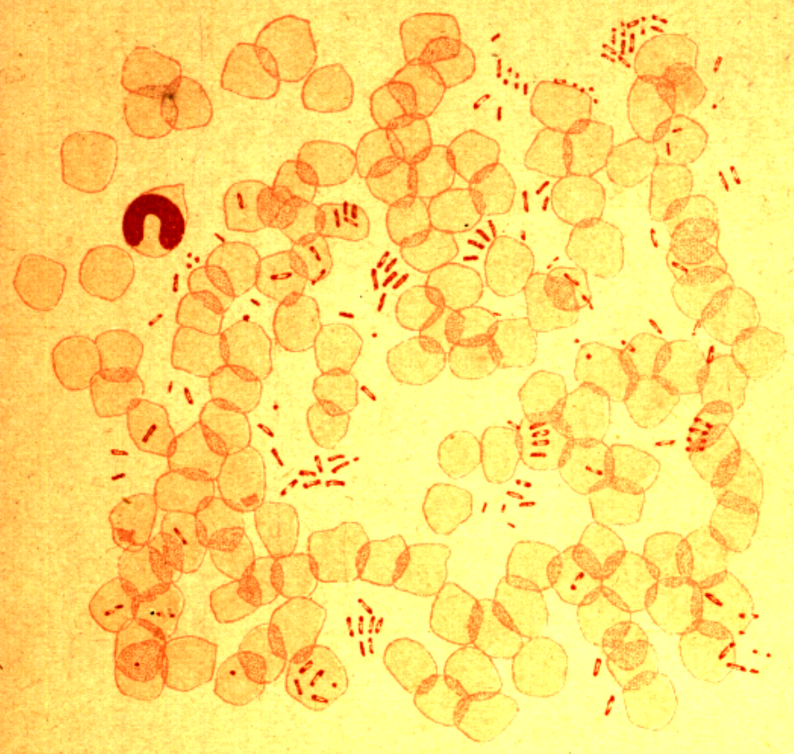
PLATE I.

Fig. 1.



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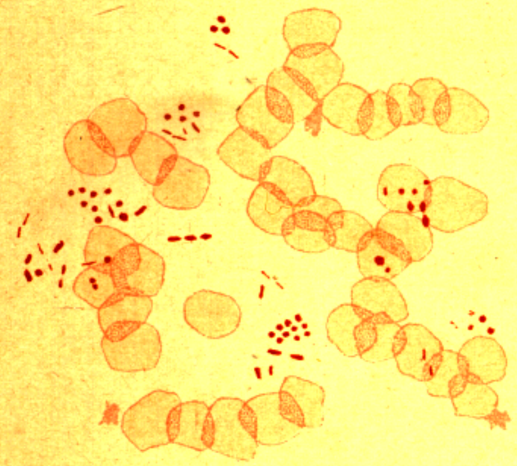

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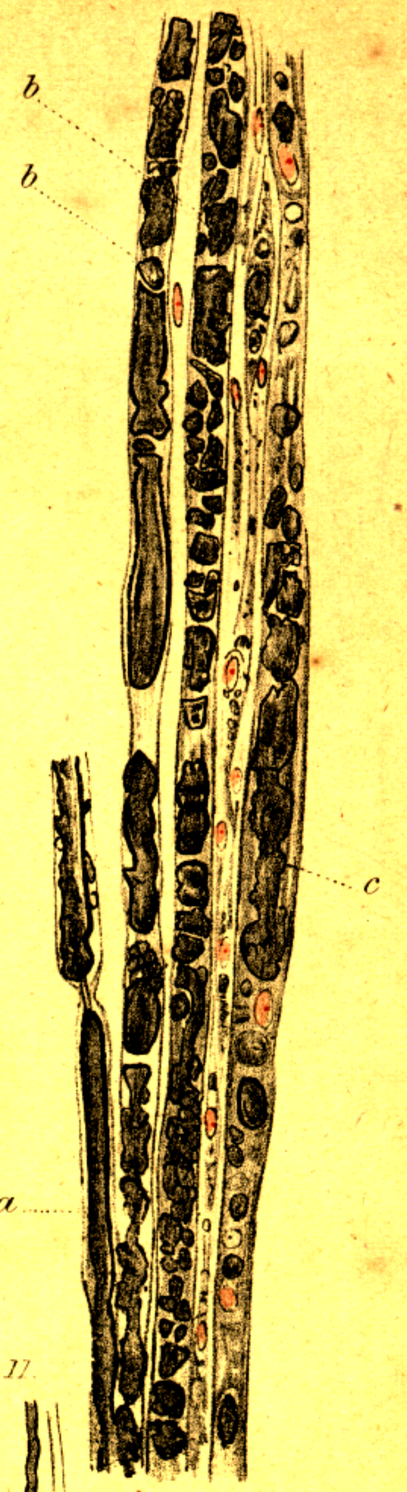


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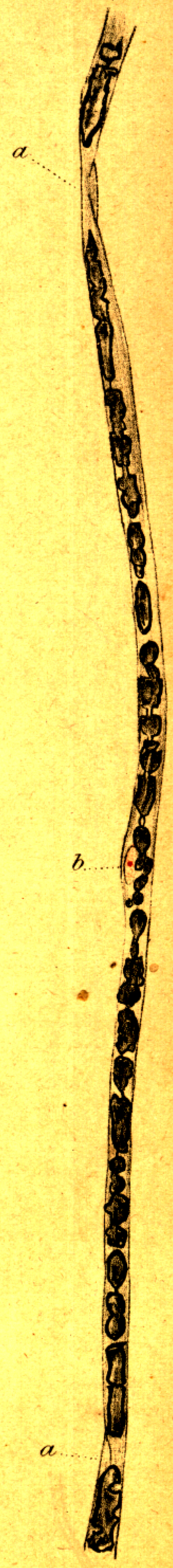



Fig. 7.

Fig. 11.

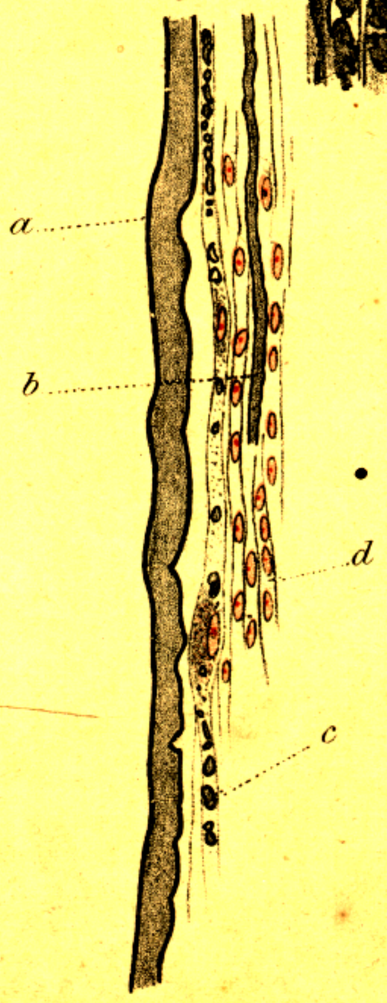
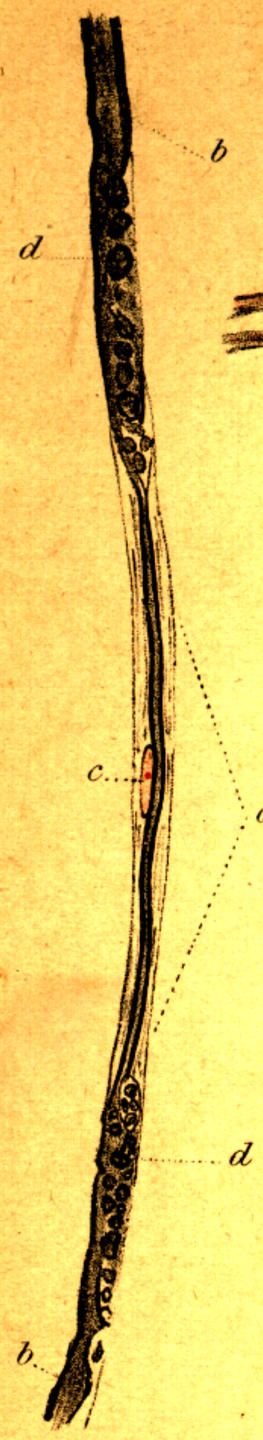


PLATE II.

Fig. 9.

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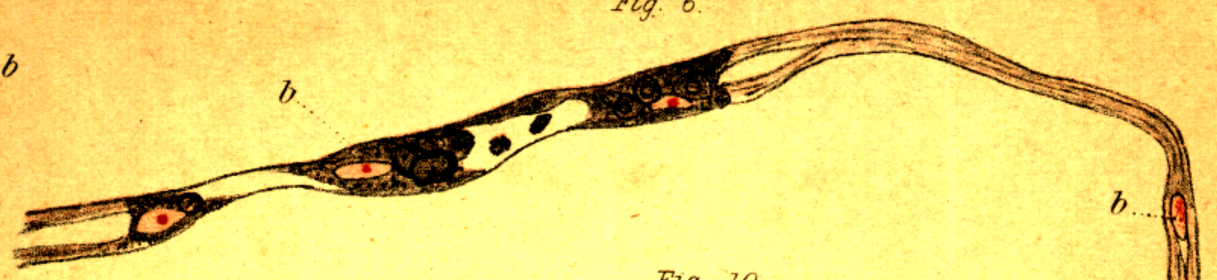



Fig. 10.

Fig. 5.

Fig. 8

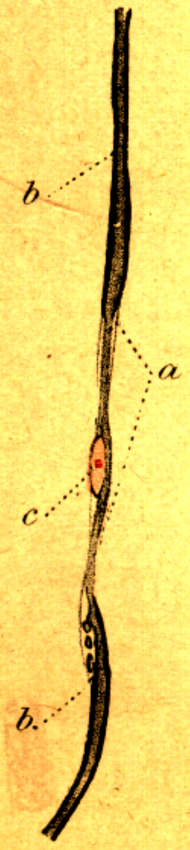
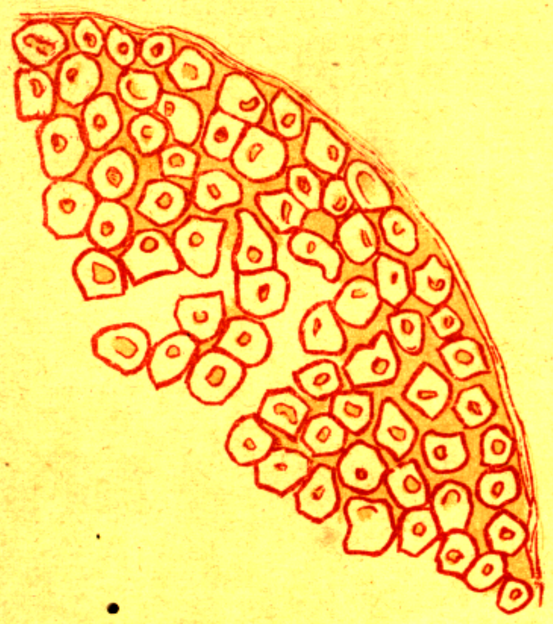


PLATE III.

*Fig 1.*

*Fig. 2.*



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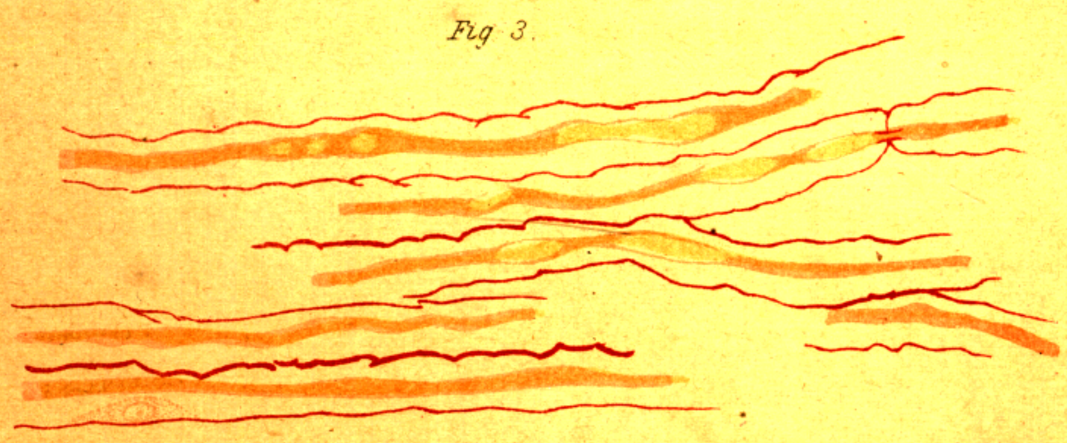


PLATE IV.

*Fig. 1.*

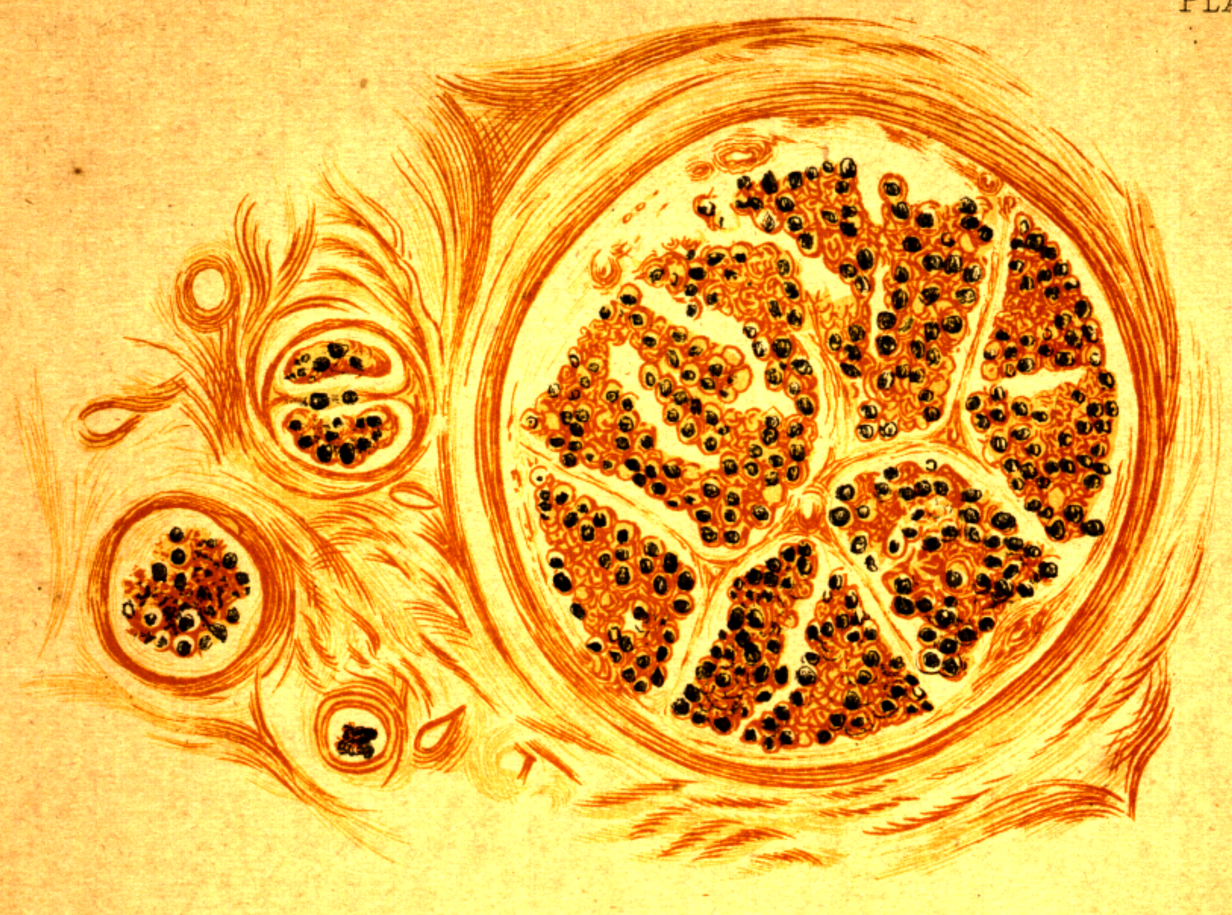


*Fig. 2.*

*Fig. 1.*

*Fig 2.*

PLATE VI.

*Fig: 1.*

*Fig 2*

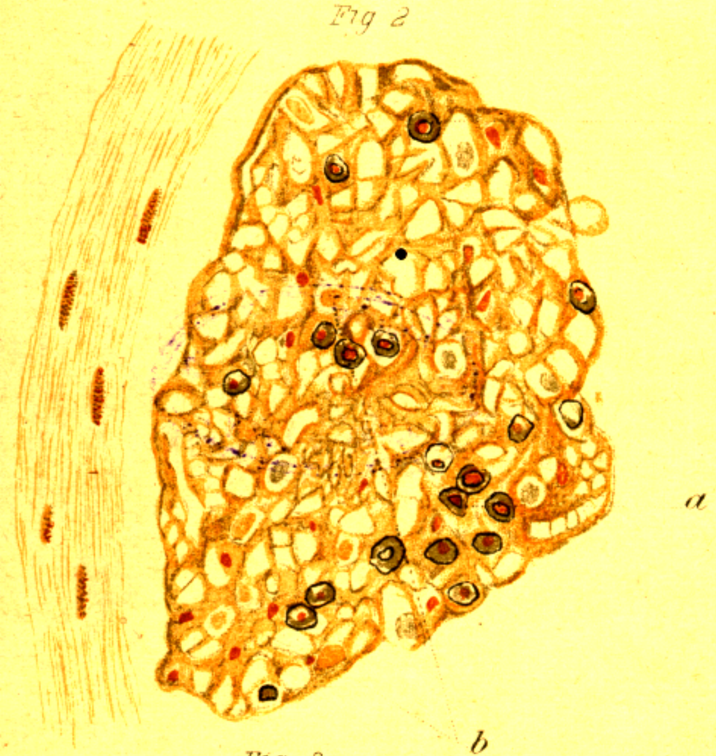



*Fig. 3*

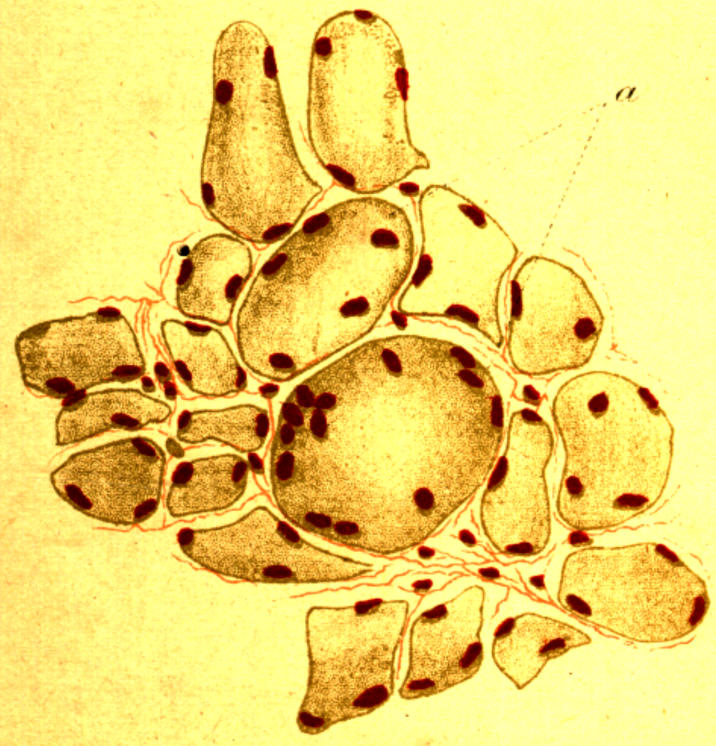


Fig. 1.

Fig. 2.

Fig. 3.

PLATE VIII.

*Fig. 1.*

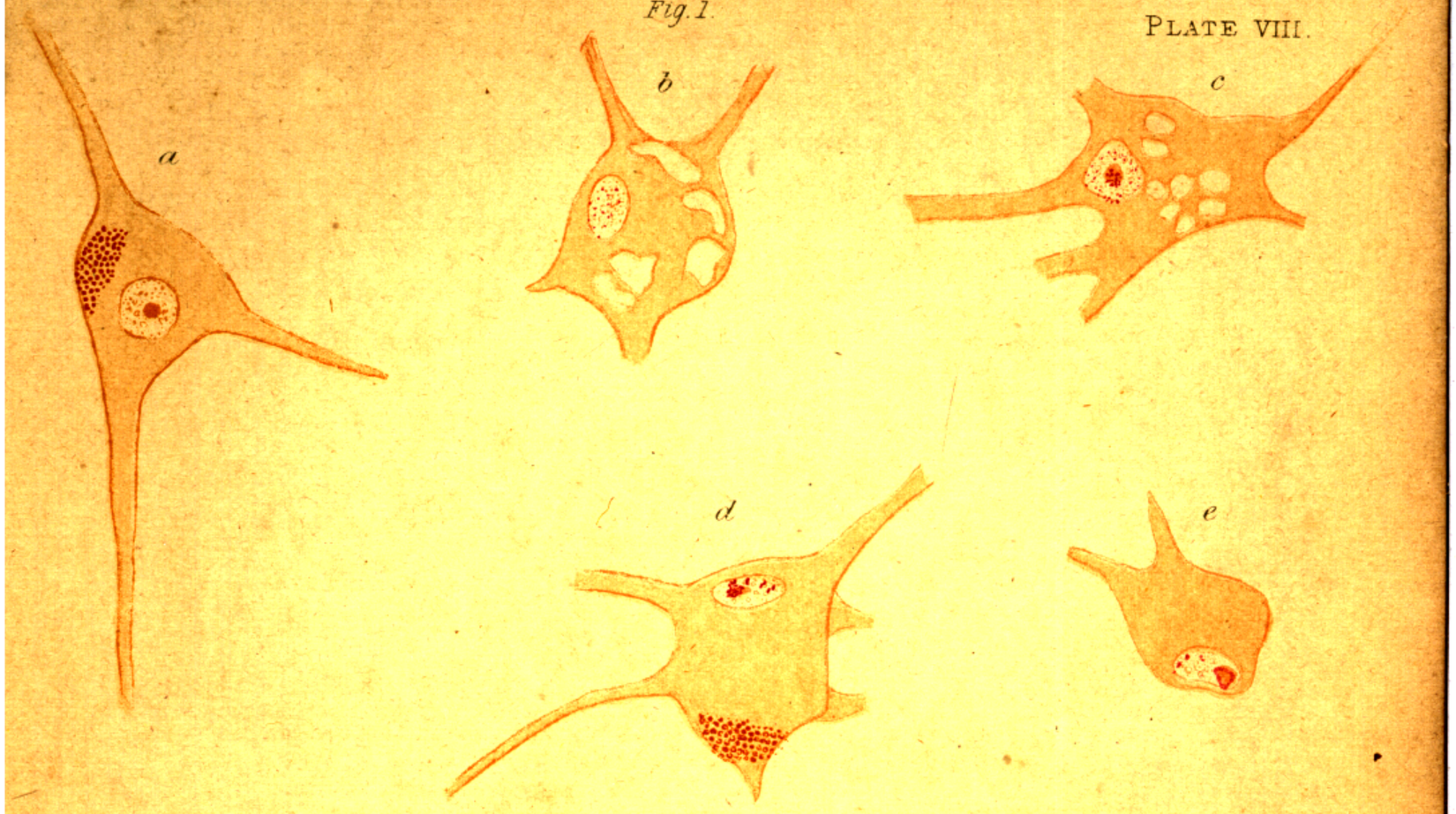



*Fig. 2.*

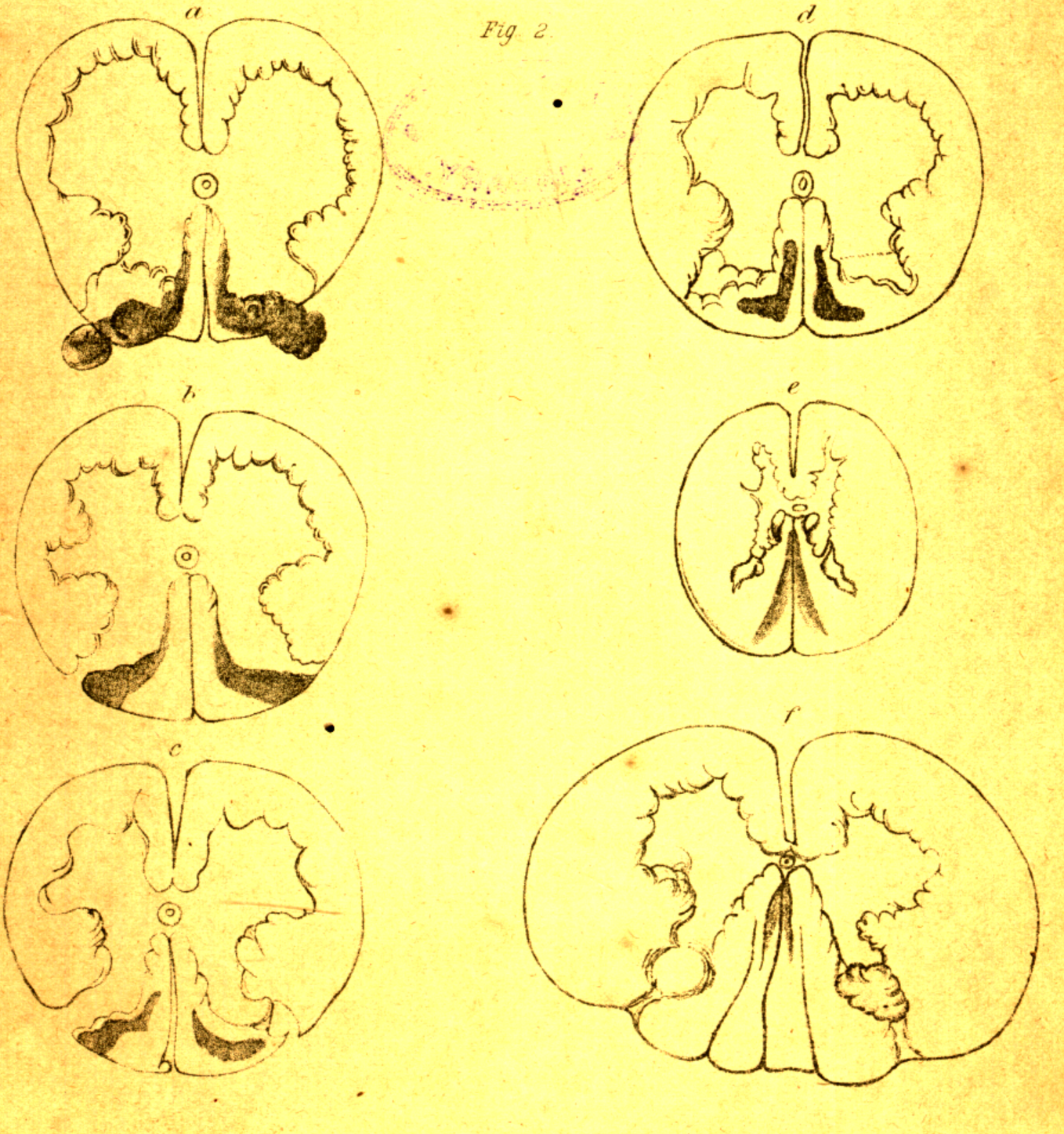


*Fig. 1*

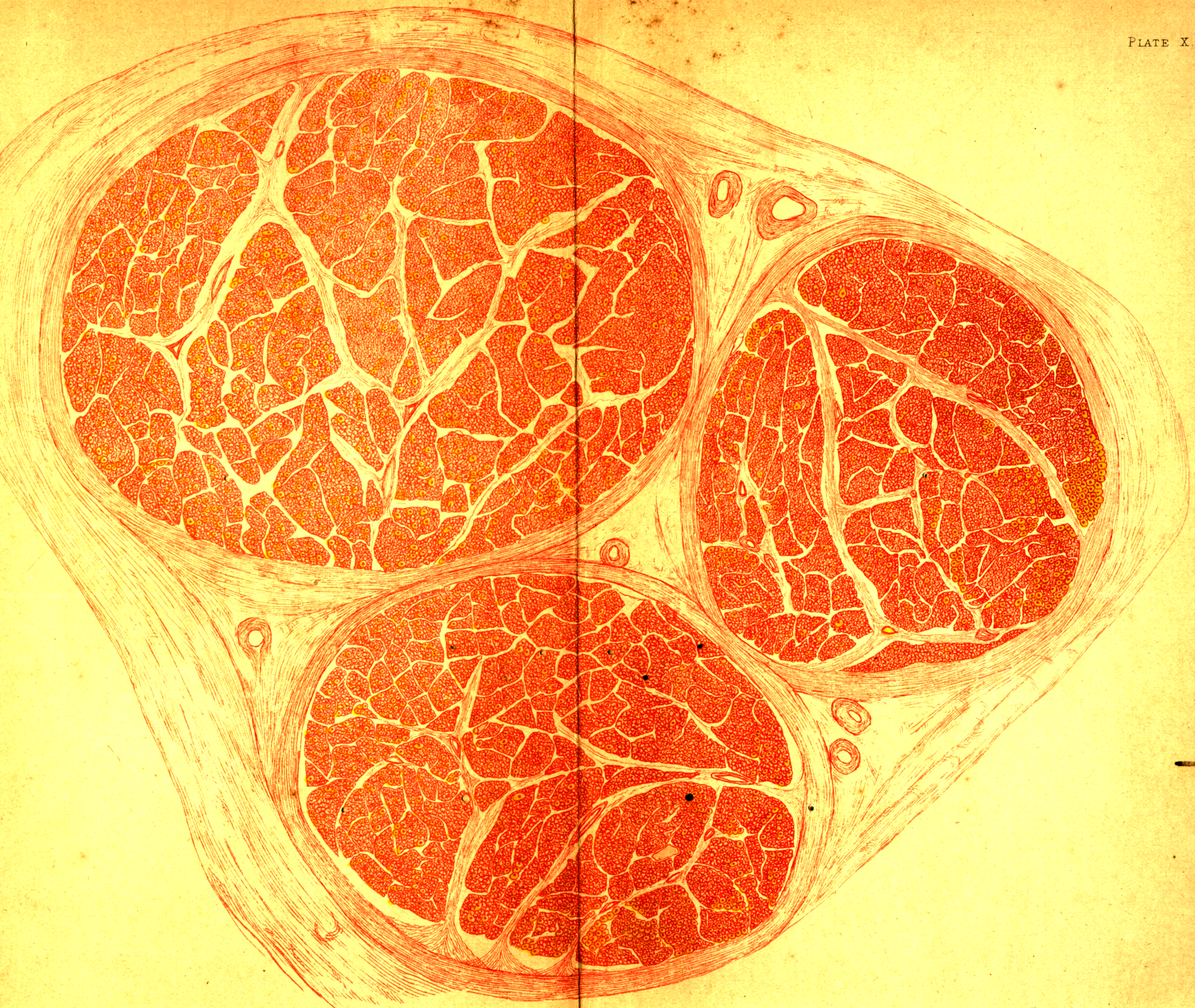
*Fig. 2*

*Fig. 3*

*a*

*Fig. 4*

*a*



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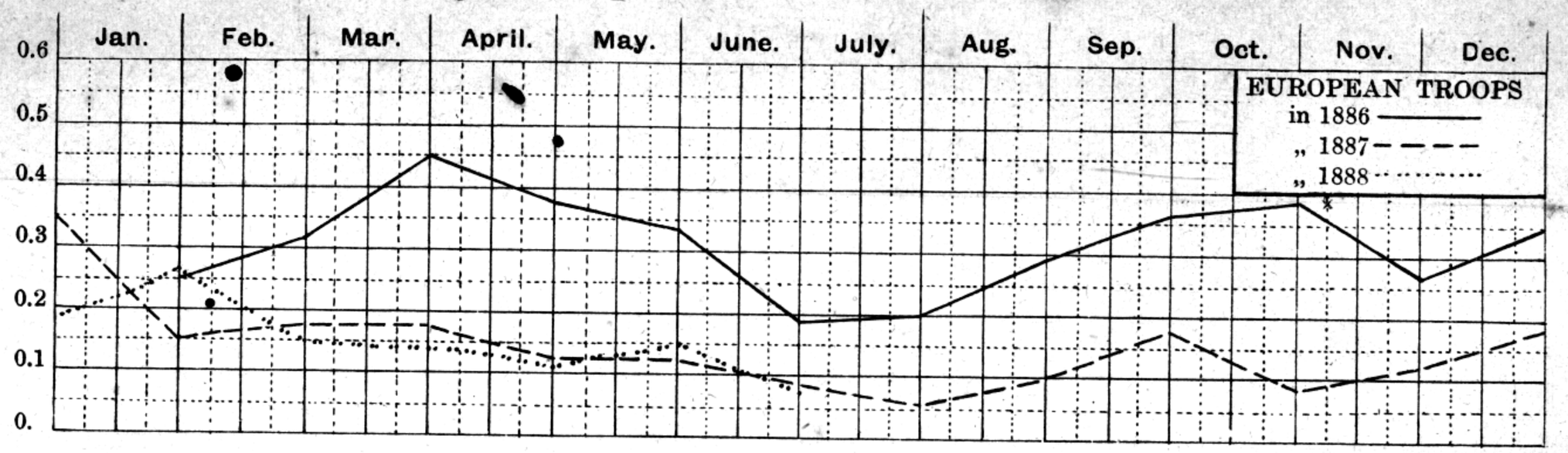


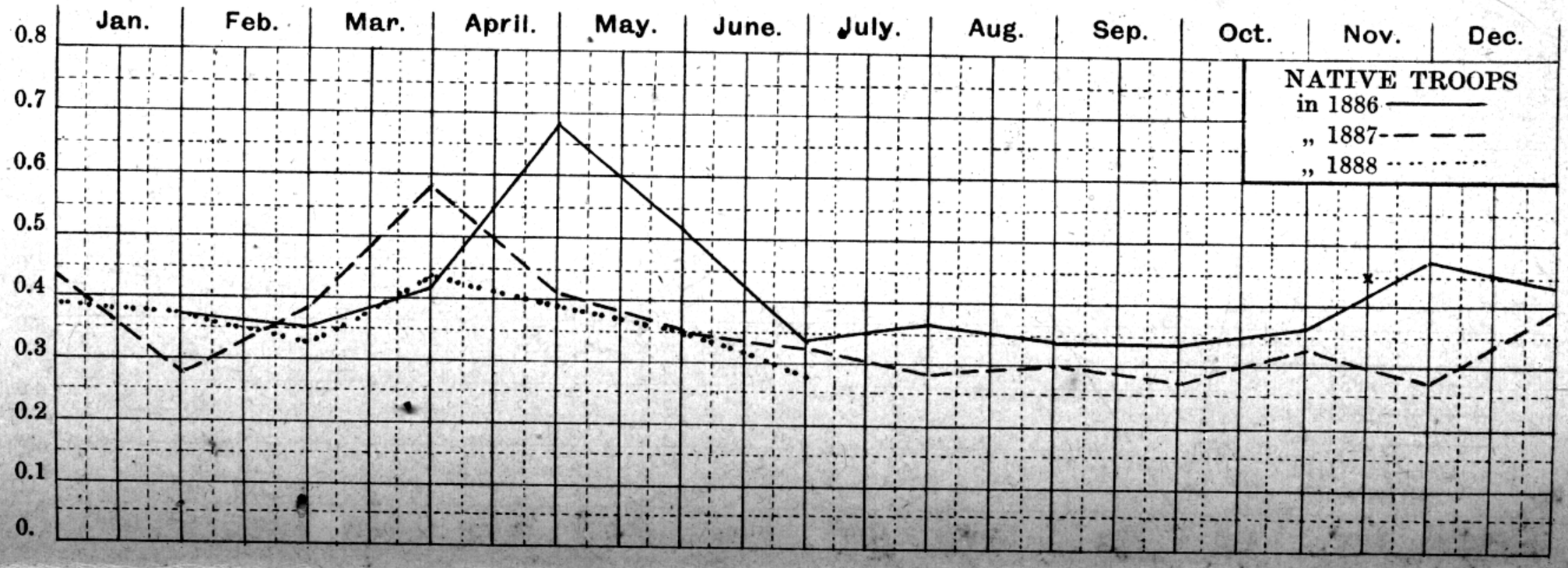


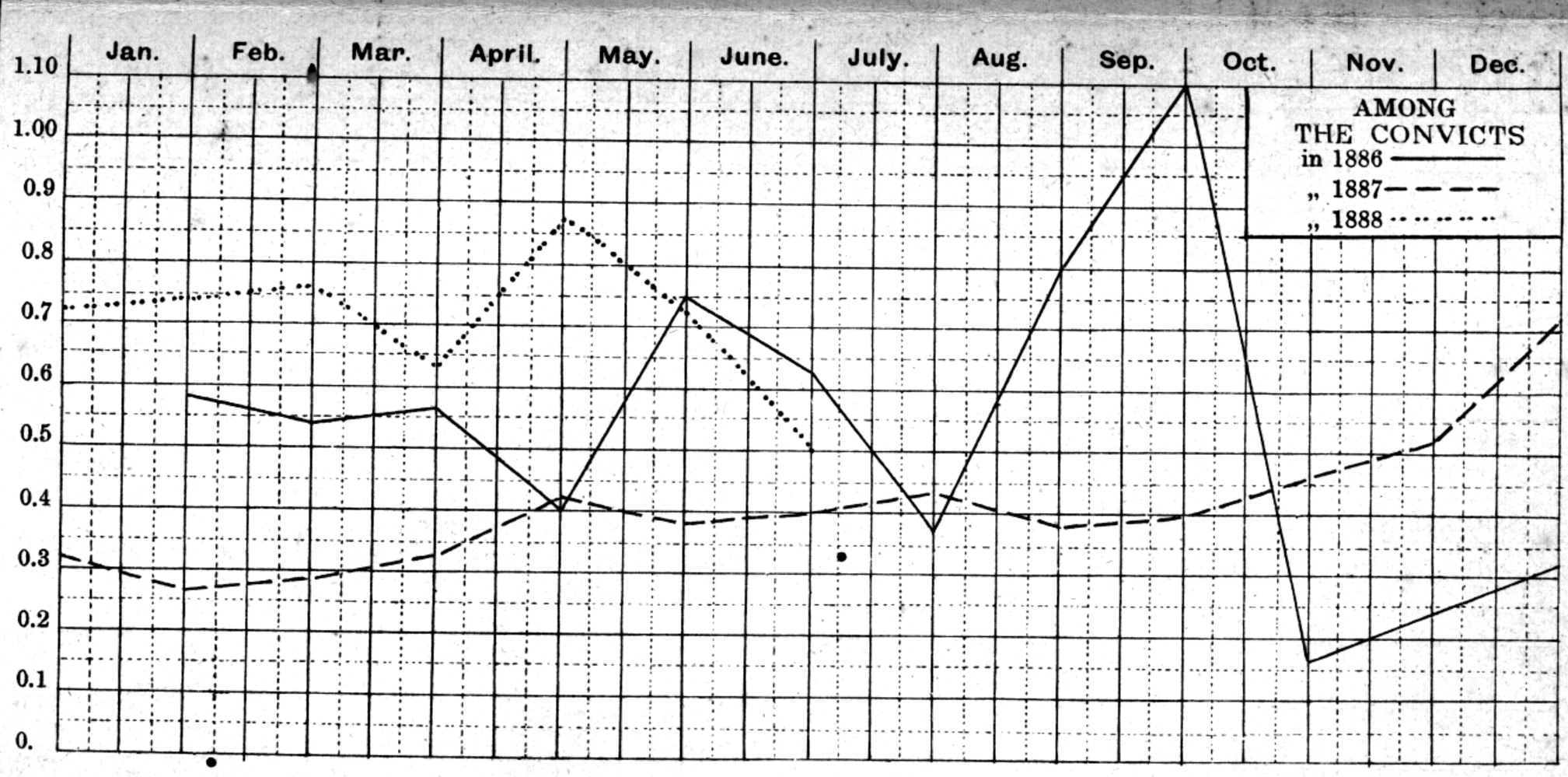


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